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VOLUME 21  
1930

PUBLISHERS  
AMERICAN MEDICAL ASSOCIATION  
CHICAGO ILL





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## EXPERIMENTAL CARDIAC VALVULAR DISEASE IN DOGS AND SUBACUTE AND CHRONIC CARDIAC VALVULAR DISEASE IN MAN

A COMPARATIVE PATHOLOGIC STUDY \*

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In a previous paper <sup>1</sup> a method was presented for creating cardiac valvular disease in dogs. The purpose of the present study is to compare the gross and microscopic structures of these experimental canine lesions with the lesions of subacute and chronic cardiac valvular disease in man.

The contention has been advanced by Swift <sup>2</sup> and others that the vegetations of subacute bacterial endocarditis are engrafted on abnormal valves and in the majority of instances, on valves that have been the site of rheumatic endocarditis. By the method previously described, <sup>1</sup> similar vegetations may be implanted on artificially traumatized valves in dogs. The chronological development of the two lesions in each case is reversed, however. In man, some form of valvular disease appears to be essential before vegetative endocarditis may occur. In dogs, fibrosis and cicatrization take place as the lesions of acute vegetative endocarditis heal.

Although the etiology of rheumatic mitral stenosis is quite different from that of experimental stenosis, in both gross and microscopic pathology, the two lesions are somewhat comparable.

### METHOD

Under ether anesthesia administered intratracheally by the Erlanger respiratory apparatus, the heart was exposed by subperiosteal resection of a portion of the left fifth rib. The electrode of a diathermy unit delivering a high frequency, bipolar current was introduced into the chamber of the left ventricle through the anterior wall. When the tip of the instrument was accurately approximated to the inferior surface of the leaflets of the mitral valve the current was applied. When the

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Submitted for publication, Dec. 19, 1929.

From the Laboratory for Surgical Research of Harvard University Medical School.

1 Powers, J. H. The Experimental Production of Mitral Stenosis. *Arch. Surg.* **18** 1945 (April) 1929.

2 Swift, H. F. The Heart in Infection, *Am. Heart J.* **3** 629 1928.

valve had been adequately traumatized, the instrument was withdrawn and the wounds were closed.

Fifty-seven operations were performed. The total operative mortality was 33.3 per cent. Eight dogs were not inoculated. Subsequent examination of the hearts of these animals showed small fibrous scars at the site of coagulation but no thickening of the leaflets of the valve and no stenosis of the orifice.

Five dogs were inoculated intravenously with cultures of *Streptococcus cardioarthritidis*. The remaining animals received cultures of *Streptococcus viridans*. All but two<sup>4</sup> developed evidence of acute vegetative endocarditis on the traumatized valve. If the acute process subsided, the leaflets became thickened and fibrosed, dense, cartilaginous scars formed around the base of the mitral ring, and frequently a real stenosis of the orifice was apparent.

Into several normal dogs were injected cultures of *Streptococcus viridans* for the purpose of control studies. When the hearts were subsequently examined, no evidence of endocarditis was found.

From the experimental material thus obtained three hearts have been selected to demonstrate the gross and microscopic structure of these lesions. From a large number of human hearts<sup>5</sup> that were studied, two have been chosen to illustrate the comparative pathologic changes.

#### PRESENTATION OF MATERIAL

*Experimental Lesions*—Dog B-30—Electrocoagulation of the mitral valve was performed under ether anesthesia. On the third postoperative day no murmur was audible. The dog was inoculated intravenously with 20 cc of a broth culture of *Streptococcus viridans*. Two days later a harsh, blowing systolic murmur was audible. The dog was injected with 80 cc of a similar culture. The following day a blood culture was taken, and *Streptococcus viridans* was obtained. The animal was killed one week after the first inoculation and the heart was removed immediately.

*Gross Description*—The heart was normal in size and consistency. The pericardium was adherent over the anterolateral border of the left ventricle at the site of the recent operative incision. No thrombi were present and with the exception of the wound in the left ventricle no myocardial abnormalities were apparent.

The aortic, pulmonic and tricuspid valves were normal.

Almost completely encircling the mitral valve was a rim of grayish, translucent, warty vegetations from 1 to 3 mm in diameter (fig 1). These lesions were friable, though firmly attached to the segments of the valve just above their free

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3 Small, J. C. The Bacterium Causing Rheumatic Fever and a Preliminary Account of Its Specific Antiserum, *Am J M Sc* **173** 101, 1927.

4 When the hearts of these two animals were examined post mortem it was evident that the electrode had been passed through the mitral orifice and placed in contact with the endocardium of the left auricle. The leaflets of the mitral valve were normal.

5 The author is greatly indebted to the Department of Pathology of the Peter Bent Brigham Hospital for the opportunity of examining these specimens and for valuable assistance in the interpretation of his observations.

margins On cross-section there was no fibrosis of the segments and no thickening except where the incision passed through a vegetation The orifice of the valve admitted the tip of the little finger

**Microscopic Description** The sections were stained with hematoxylin and eosin, Giemsa and Goodpasture stains The section included a small portion of both the auricular and the ventricular walls and a complete segment of the mitral valve Except for some edema of the auricular wall, the myocardium of both auricle and ventricle was normal As it approached the mitral valve, the endocardium became thickened, and a pronounced cellular response was evident in an area of considerable size at the base of the leaflet This cellular infiltration extended for some distance along the subendocardium of the ventricle and consisted almost entirely of polymorphonuclear leukocytes On the ventricular aspect of the base of the valve was a superficial area of myocardial necrosis with early fibroblastic proliferation into the periphery Hemosiderin was quite prominent A considerable amount of hemorrhage was present

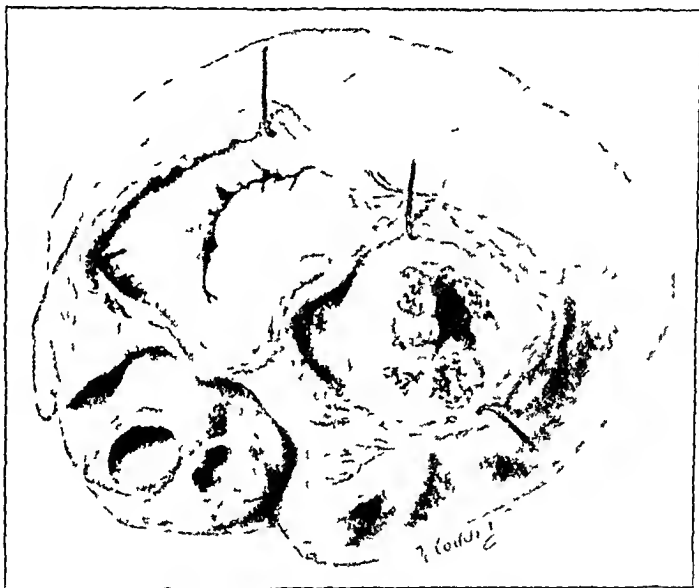


Fig 1—Experimental vegetative endocarditis produced by electrocoagulation of the mitral valve and intravenous inoculation with cultures of *Streptococcus viridans* in dog B-30 The animal was killed one week after the first inoculation

The mitral valve itself was greatly altered From the widened valvular base, which was heavily infiltrated with polymorphonuclear leukocytes and in which areas of necrosis were visible (fig 2), the valve approached more normal thickness until the distal half was reached Here the endocardium was almost replaced by a large thrombus Only a few strands of necrotic fibrous tissue were apparent A heavy infiltration of polymorphonuclear leukocytes had occurred into the remaining substance of the valve

While a considerable portion of the degenerative changes in the valve was probably due to coagulation, there were numerous thrombi with large numbers of inflammatory cells which were characteristic of bacterial injury In fact, examination of identical sections through the valve of another heart revealed several clumps of bacteria embedded in the thrombi (fig 3)

**Dog B-19**—Electrocoagulation of the mitral valve was performed with the dog under ether anesthesia During the next three weeks a transient, soft sys-



toic murmur was audible. The dog was in good health. Subsequently the murmur disappeared and the animal was reoperated on six weeks after the first procedure. Two intravenous inoculations with *Streptococcus viridans* were administered, and this organism was recovered in pure culture at intervals until death. One month after the second operation auscultation of the heart revealed a moderately loud systolic murmur, no second sound and a short early diastolic rumble. The dog gradually became lethargic, would not stand, refused food and water, and died on the forty-second postoperative day. The heart was not removed until several hours later.



Fig 2—Microscopic appearance of the base of the mitral valve shown in figure 1. The section shows granulation tissue on the surface of the valve, myocardial necrosis, and a heavy infiltration of inflammatory cells into the subendocardium.

**Gross Description.** The heart was of normal consistency and showed a healed incision on the anterior surface of the left ventricle. The various chambers of the heart were free from thrombi, and the valves, with the exception of the mitral, were normal.

When examined from above, the mitral valve showed remarkably thickened segments and on palpation would not admit the tip of the little finger (fig 4). The mitral orifice presented an irregularly oval opening which was slightly over-

lung by a thickened, contracted ridge of auricular endocardium about 3 mm above the margin of the valvular segments

On cut section the valve was thickened, especially along the free margin, and tough and fibrous in consistency

**Microscopic Description** The section included a portion of the auricular and ventricular walls and the entire mitral leaflet. The area of involvement was



Fig 3—Clumps of bacteria embedded in a thrombus

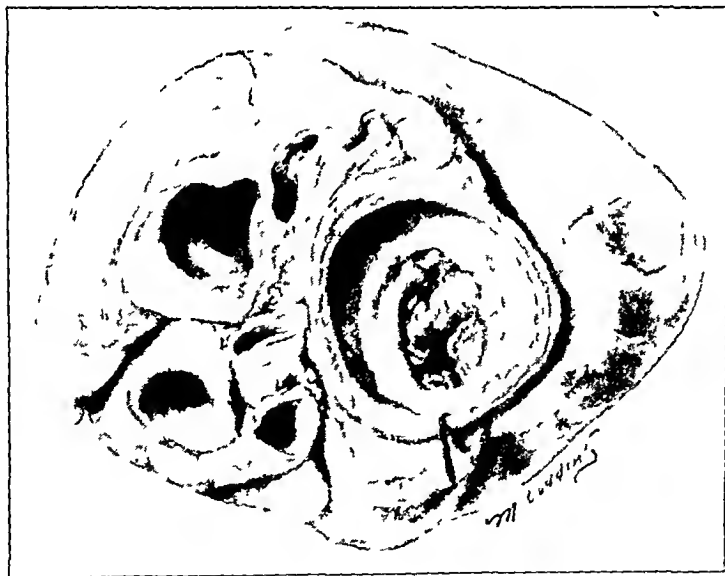


Fig 4—Experimental mitral stenosis in dog B-19. The segments of the valve are thickened and the orifice does not admit the tip of the little finger. The animal died of cardiac failure six weeks after the onset of acute endocarditis.

approximately the same as in the heart previously described. A notable difference in the two sections, however, was at once apparent in the amount of organization that had occurred. At the base of the valve was an extensive proliferation

of fibrous tissue with the formation of fibrocartilage at the junction of the inferior surface and ventricular endocardium. New blood vessels were prominent about the outer limits of this dense scar tissue and fibroblastic proliferation was evident. Enclosed within the scar tissue at the base of the valve was a necrotic mass of formless material in which no cellular elements were recognizable. The sub-endocardial granulation tissue on both auricular and ventricular surfaces was carried out onto the tremendously thickened valvular leaflet, and in most fields small, thin walled blood vessels were seen embedded in the fibrous tissue. On the distal end of the valve there was still some formless necrotic material in which hemosiderin was found.

Dog B-25—Electrocoagulation of the mitral valve was performed under ether anesthesia. A soft systolic murmur was audible after the operation. One month later the dog was given two intravenous inoculations with cultures of *Streptococcus viridans*. Subsequently, the murmur was slightly accentuated. The animal was reoperated on and reinoculated twice with 100 cc of a similar culture. One week later this organism was recovered from the blood stream.

Three months after the second operation, auscultation of the heart revealed reduplication of the second sound but no definite diastolic murmur. The dog was in good health. The blood culture was negative. The animal was killed four months later, and the heart was removed immediately.

Gross Description. With the exception of the mitral valve the general appearance of the heart was identical with that of the preceding one.

When examined from above the mitral orifice was reduced in caliber and did not quite admit the tip of the little finger. At the anterior junction of the aortic and lateral segments a somewhat polypoid puckered, cartilaginous nodule was apparent. The aortic segment and midportion of the lateral segment were markedly sclerosed and measured 3.5 mm in thickness. On the scarred margin of the lateral segment was a hard, smooth, cartilaginous nodule 3 mm in diameter. This appeared to be a healed vegetative lesion because of its intimate relationship to the puckered, scarred, valvular margin.

The aortic segment was much thickened, tough and fibrotic (fig 5). On the inferior surface, at the junction with the ventricular endocardium, was a small, cartilaginous nodule similar to that on the superior surface of the lateral segment.

In cross-section both lateral and aortic segments presented a fusiform contour with the greatest thickening in the proximal third just distal to a slight constriction at the base (fig 6).

Microscopic Description. The tissue was taken from the specimen shown in cross-section in figure 6. Portions of the auricle and ventricle and the entire aortic segment were included. There was no residual exudate on the valve. The leaflet was markedly fibrotic and presented a fusiform thickening of the inner half largely due to the replacement and ingrowth of fibrocartilage. There was also a large area of fibrocartilage near the base. The cartilaginous character of the tissue was manifested by the presence of typical, clear cells embedded in a deeply basic staining matrix (fig 7). At the borders of these cartilaginous areas there was a gradual transition into dense acellular connective tissue. Vascularization was apparent on the superior surface of the leaflet, where several pre-capillary sized blood vessels were seen.

Human Lesions—CASE A-29-3—A white woman, aged 34 was brought to the hospital because of bronchopneumonia and diabetes mellitus. The history disclosed the fact that she had been treated for cardiac valvular disease of rheu-

matic origin eleven years previously. Physical examination of the heart was unsatisfactory because the sounds were obscured by harsh breathing and a loud, pleural friction rub. The patient was moribund on admission and died a few hours later. Necropsy was performed.



Fig 5—Experimental mitral stenosis in dog B-25. Both segments of the valve are markedly thickened and sclerosed. The orifice would not admit the tip of the little finger.

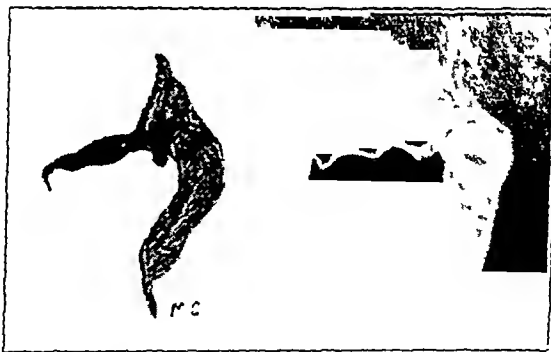


Fig 6—Vertical section through the aortic segment of the stenotic mitral valve shown in figure 5, and through a normal valve for comparison. The valve at the left is densely scarred and thickened, at its base is a firm cicatrix composed largely of fibrocartilage.

**Gross Description of Heart** The heart was moderately hypertrophied and dilated and weighed 395 Gm. The myocardium of the left ventricle measured 15 mm in thickness, that of the left auricle, 4 mm. The right side of the heart showed no abnormality.

There was some thickening and fibrosis of all the segments of the aortic valve. The endocardium of the left auricle showed several roughened and puckered areas. The mitral valve presented the characteristic appearance of moderate stenosis with superimposed vegetative endocarditis. When examined from above, the orifice admitted only one finger. There were several grayish red warty vegeta-

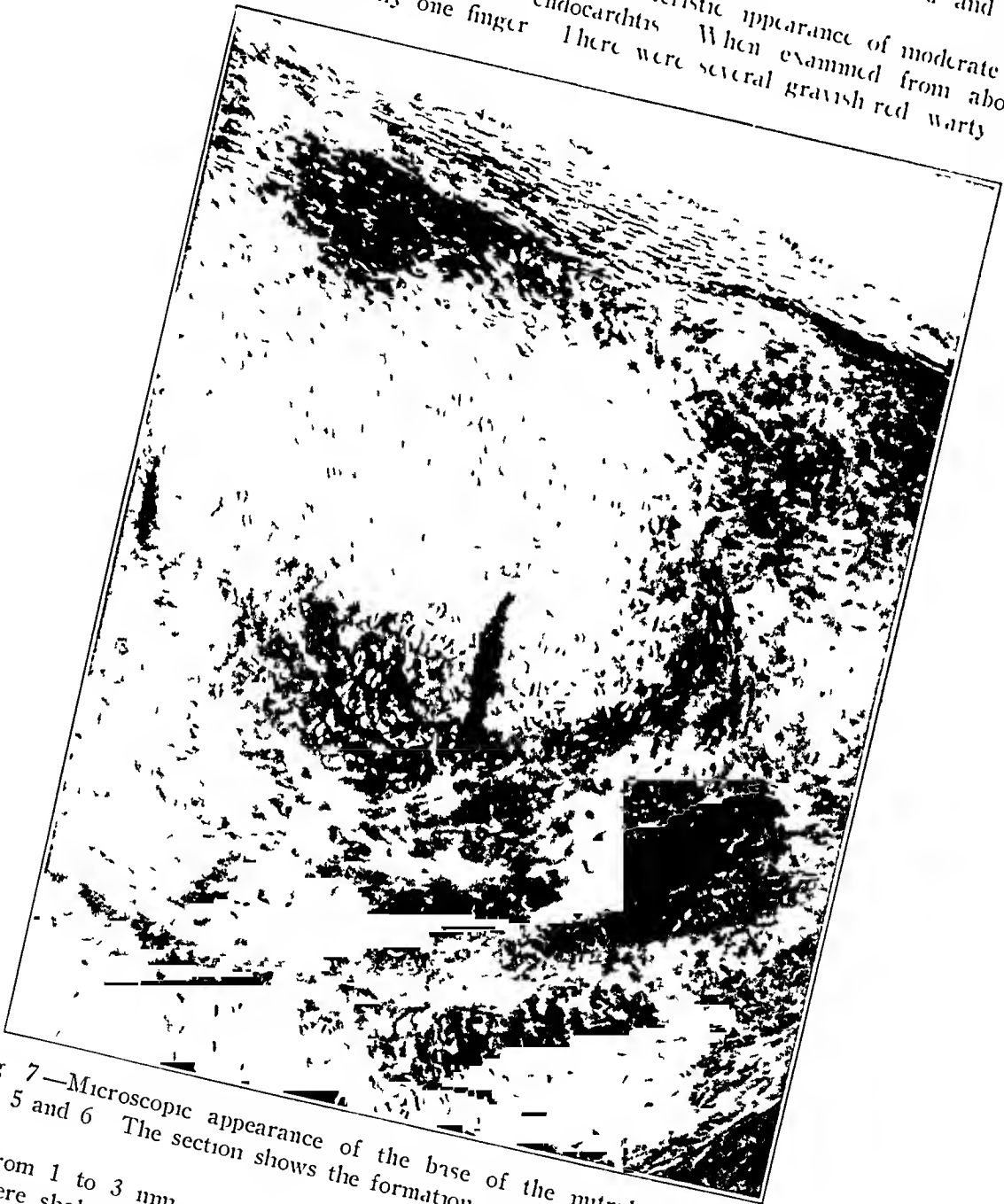


Fig 7—Microscopic appearance of the base of the mitral valve shown in figures 5 and 6. The section shows the formation and ingrowth of fibrocartilage

tions, from 1 to 3 mm in diameter, along the margin of the lateral segment. They were slightly friable but were not easily broken away from the endocardium. A noteworthy feature was the presence of numerous capillaries forming a veil-like network over the valvular endocardium (fig 8). (These vessels have been rendered prominent by injection of the coronary circulation with a suspension of bismuth subchloride in acacia.) On cut section the valve was thickened throughout its length, especially in the distal half, where it measured 3 mm (fig 9).



Fig 8—Mitral stenosis of rheumatic origin in case A-29-3, showing vascularization of the valve and superimposed vegetative endocarditis. The vessels have been rendered prominent by injection of the coronary circulation with a suspension of bismuth subchloride. (Compare the gross appearance of this valve with that shown in figure 5.)



Fig 9—Vertical section through the valve shown in figure 8. There is a marked increase in the thickness of the segment. (Compare with figure 6.)

**Microscopic Description** The histologic examination included a cross sectional study of the entire mitral valve and portions of the adjacent auricular and ventricular walls. In the ventricular myocardium at the base of the valve there was a wide area of scar tissue with fibrous bands running out for great distances between individual muscle fibers and bundles of cardiac musculature. A scattering of lymphoid and plasma cells persisted in this fibrous tissue. Near the base of the valve were numerous cicatrices about small blood vessels. In



Fig 10—Severe mitral stenosis with marked thickening and scarring of the entire valve in case A-29-14 (Compare with the experimental lesion shown in figure 4)

some instances these scarred areas were quite heavily infiltrated with lymphoid cells and endothelial phagocytes.

The mitral valve itself was long and uniformly thickened. The endocardium was intact except at the tip, where a small organizing thrombus was attached. Capillary and precapillary sized blood vessels were prominent throughout the entire length of the valvular leaflet. The valve itself was devoid of cellular infiltration, it was dense and fibrous. The subendocardium on the auricular side was more prominently thickened than was that on the ventricular aspect.

CASE A-29-14—A white man, aged 48, entered the hospital because of edema of the ankles, dyspnea and precordial pain. The history revealed the fact that he had had rheumatic fever at the age of 18 and again at the age of 28. Physical examination showed cardiac enlargement, a presystolic thrill, a rough presystolic murmur, and a loud snapping first sound. There were signs of fluid at both bases. The patient died of cardiac failure.

**Gross Description** The heart was markedly hypertrophied in all chambers and weighed 495 Gm. The myocardium of the left ventricle measured 18 mm in thickness, that of the right ventricle, 6 mm, the left auricle, 6 mm, and the right auricle, 4 mm. In addition to the hypertrophy, there was marked dilatation of all chambers, especially of the left auricle and to a less degree of the right auricle.

The pulmonic valve was normal. The aortic valve showed thickening of its segments with fusion of the anterior and right lateral cusps. At this point there was also some calcification. The tricuspid valve was moderately thickened and stenosed. The orifice admitted only the tips of two fingers.

The mitral valve was of the "fish mouth" variety and would not admit the tip of the little finger (fig 10). The orifice was crescentic in appearance and measured 7 mm by 1 mm in its greatest dimensions. There was marked wrinkling and puckering of the entire valve and to a less extent of the endocardium of the left auricle. A small, friable thrombus was attached to the auricular wall on the interauricular septum. One circumscribed cartilaginous elevation was present on the aortic segment. No vegetations were apparent.

**Microscopic Description** The histologic appearance of the mitral valve was similar to that described in case A-29-3. Thickening of the valvular segment was more pronounced, and small blood vessels were more numerous. There were also a few small foci of round cells embedded in the dense fibrous substance of the valve. There was no remaining cellular response in the myocardium of the adjacent auricular or ventricular walls.

#### SUMMARY AND CONCLUSIONS

The vegetations of acute endocarditis produced experimentally in dogs by electrosurgical traumatization of the mitral valve and subsequent intravenous inoculation with cultures of *Streptococcus viridans* are similar to the vegetations of subacute bacterial endocarditis in man. In some cases it is possible to demonstrate microscopically clumps of bacteria included within the thrombi. Some of the larger areas of necrosis which occur in the experimental lesions may be attributed to the coagulation of tissue produced by the operative procedure. Heavy infiltration of inflammatory cells occurs in both types. In the more chronic experimental lesions, repair occurs by avascular cicatrization, in the human lesions, vascular organization is usually more prominent. The human hearts show more shortening of the cordae tendineae and a more diffuse, complete involvement of all the segments of the valve.

In the favorable canine lesions which go on to complete healing fibrocartilage is laid down. A thickened fibrous valve is produced which is somewhat comparable to mitral stenosis of rheumatic origin in man.



# HEREDITARY DEFORMING CHONDRODYSPLASIA\*

REPORT OF A CASE

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Considerable interest has recently been aroused concerning a disease entity of the skeleton which has been referred to most commonly as multiple cartilaginous exostoses. Certainly the manifestation of interest in the disease in America can be said to be recent for the first case reported in this country was by Gibney<sup>1</sup> in 1875. Not unlike most disease entities of the skeleton, this disease has been given a name by almost every author who has written about it. Like practically all of the hereditary disease entities of the skeleton, its etiology remains a mystery.

It is not within my province in this paper to discuss in detail the disease itself, for this has been adequately done in a number of relatively recent papers particularly in that of Albert Ehrenfried.

The studies here are devoted to three aspects of the disease: (1) a brief study of the disease as represented by the case reported in this paper, including the hereditary and familial features; (2) a consideration of the changes that occurred in one of the tumors and that suggested malignancy; (3) a comparative study of this disease with chondrodystrophia fetalis.

Hereditary deforming chondrodysplasia is characterized by a number of definitely recognized features. It is hereditary and familial having been traced through five generations in several instances. Both males and females may transmit the disease and while it may be transmitted by an unaffected female, there is no evidence that it can be transmitted by an unaffected male. It has been recorded that two mothers had affected children by different husbands, and that one father had affected children in two marriages. There is a tendency to conform to the mendelian law of inheritance, and males predominate in the proportion of 3:1.

In attempting to find an etiologic factor, Virchow and others have considered the condition secondary to rickets. However, aside from the fact that the microscopic cross-section of the diaphysis and epi-

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\* Submitted for publication, Feb. 3, 1930.

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1 Gibney, V. P. Multiple Exostoses, *Med. Rec.* **10**: 300, 1875.

2 Ehrenfried, A. Hereditary Deforming Chondrodysplasia—Multiple Cartilaginous Exostoses. A Review of the American Literature and Report of Twelve Cases, *J. A. M. A.* **68**: 502 (Feb. 17) 1917.

physis presents a considerably different picture in the two disease entities, there are certain clinical facts which also militate against this possibility. Among the numerous instances of recognized rickets, this chondrodysplasia is not seen to occur, and so far as my observations have been concerned, certain characteristics which show up in rickety bone ends, such as the parallel transverse lines of increased density, are lacking in this disease. Furthermore, the pathologic change in rickets consists essentially in the production of osteoid tissue with a deficiency in calcification whereas here one is dealing with a distorted, unregulated line of ossification and sometimes indeed with a premature ossification of the intermediary cartilage. The latter probably accounts for some of the shortening of the extremities and has suggested to some a resemblance to chondrodystrophia fetalis. Again, the treatment for rickets is a well recognized and standardized therapeutics affecting a cure, whereas similar treatment has no curative or abating effect on the disease in question. Histologic studies have been made which bear adequate witness against an identity of the two diseases.<sup>3</sup> Other etiologic factors that have been mentioned are the thyroid gland, a trophic disturbance due to a degenerative disease of the nervous system and syphilis and tuberculosis.

Although the primary factor is not established, it would seem to me that at least one fact is tenable and clear, that cartilage rests are left in the wake of a chaotic advancing epiphysis, and these rests undoubtedly form the nucleus of the anomalous benign tumors. Ehrenfried's microscopic studies of such epiphyses and bones bear this out, and, of course, whether one encounters a sessile tumor on the shaft or a central tumor expanding the cortex depends on the location of the cartilage rest.

Sir Arthur Keith,<sup>4</sup> carrying the analysis further and offering a somewhat different explanation, maintained that a retardation or absence of the pruning and modeling process in the diaphysis is the responsible factor, and he proposed the name "diaphysial aclasis" to designate the disease.

Briefly, the disease may manifest itself in any of the bones formed from cartilage but not in intramembranous bones. Hence the cranium is seldom affected. An occasional exostosis and spur have been reported as occurring on the cranial vault and from the basilar process at the sphenoccipital junction, but by far the more common observation in all the case reports studied is a normal cranium.

3 Pels-Leusden. Klinische, pathologisch-anatomische und radiologische Studien über Exostosis cartilaginea multiplex, Deutsche Ztschr. f. Chir. **86** 434, 1907.

4 Keith, A. Studies on the Anatomical Changes Which Accompany Certain Growth Disorders of the Human Body. J. Anat. **54** 101, 1919.

Interesting complications have been reported owing to the location of the growth and mechanical pressure. Outstanding examples are those which cause neurologic symptoms due to pressure on the spinal cord and intrapelvic growths causing dystocia in the birth canal.

Dr. Boggs,<sup>5</sup> in 1913, reported an interesting case in which the patient presented an optic and acoustic nerve degeneration but he concluded that these were not attributable to the skeletal disease. Dr. Bloodgood in a discussion mentioned two of his collected cases in which the lesions showed cyst formation. He stated further that multiple enchondromas and exostoses are the only two congenital lesions of the skeleton producing cyst formation. Other diseases mentioned which produce cyst formation are osteitis fibrosa (von Recklinghausen's disease), osteitis deformans (Paget's disease), osteomalacia and mercurial poisoning. He also stated that no examples of malignant degeneration had been observed in multiple congenital osteochondromas.

The tumors have been reported present at birth and appearing as late in life as the age of 50, although it is more common to find their growth coincident with that of the normal bone. Recession in growth after puberty has also been reported.

Among the many varied and interesting characteristics of the tumors themselves as they occur in the various enchondrial bones, which have been discussed in detail by Eichenfried, is the peculiar distorted development of the ulna and fibula, particularly as compared with that of the radius and tibia, respectively. The lower end of the ulna and both ends of the fibula may be lacking considerably in necessary length, ending with a distorted, perhaps squared or rounded off end, presenting a foam-like roentgenographic appearance. The disproportionate development of the two bones in the forearm and in the leg gives rise to a distorted and crippled appearance of the extremities, particularly of the hands such as *manu vara*, dislocation of the head of the radius and a weak wrist joint. An adequate explanation of these almost constant proportions has not been made. A comparison of the times of ossification and union of the epiphyses does not offer enough discrepancy to arouse interest. (The heads of the ulna and radius ossify at the tenth and fifth years and unite at about puberty. The distal ends ossify at the fourth and second years and unite at the twentieth year. The heads of the tibia and fibula ossify shortly after birth and about the fourth year, respectively, and unite at the twentieth and twenty-fifth years. The distal ends ossify at the second year and unite at the eighteenth and twentieth years.)

A possible explanation for this interesting deformity which occurs where two bones are in juxtaposition, as in the forearm and leg, may

be found in the diversion of the normal epiphyseal growth. In the instances in which one of the two bones has stopped short of its normal growth and one of its ends presents a stublike deformity as if part of the bone had been melted away, one sees proximal to this an enchondroma abutting the shaft of the adjacent bone. In some cases the latter, apparently reacting to the stimulus of the former, throws out a bulwark of bone to meet it. The resulting picture is that of a pseudo-joint, and thus it is not illogical to assume that in this way the normal linear epiphyseal growth is distorted laterally and the stimulus for linear growth stunted if not completely lost. How this factor could play such a role in both the forearm and the leg is shown in figure 1, taken from McFarland's report of a case.<sup>6</sup> It can also be seen in the case presented here (figs 4 and 7).

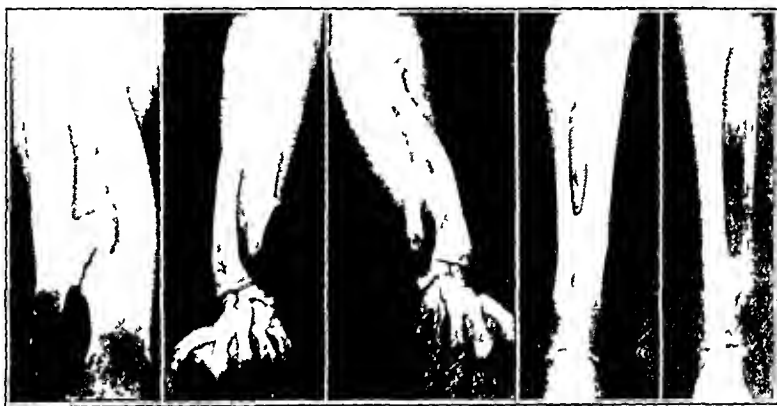


Fig 1—Roentgenograms of the arms and legs of McFarland's patient (Surg Gynec Obst 48 268, 1929). Note the effect of pseudo-joint formation on the growth of the ulna and fibula.

The tumor itself varies in its content of bone, but is practically always less dense than the adjacent normal bone. If it is centrally located, it expands the cortex. Roentgenologically, it presents the "lace curtain effect" or "foamlike" structure, resembling in some ways the giant cell tumor of bone. Delicate bone septums encase the less dense cartilaginous tissue. Although these tumors may grow to an enormous size, in a roentgenogram they present only in rare instances an appearance that is the least suggestive of malignancy such as is found in sarcoma of the bone.

#### REPORT OF CASE

*History*—Daniel T., a white man, aged 48, a native of Iowa, first entered the University Hospital on June 30, 1927, with a complaint of a slightly painful tumor of the right hip. The patient's father was of Irish descent and died of pneu-

<sup>6</sup> McFarland J. Hereditary Deforming Chondrodysplasia, Surg Gynec Obst 48 268 1929.

monia at the age of 67. He was 5 feet, 2 inches (153 cm) tall and presented what the family referred to as the "Toher mark" (short extremities and an inability to extend the forearms fully). It is interesting that the hereditary nature of this disease has been so impressed on the family for at least three generations that it has been referred to as the 'Toher mark,' the family name being Toher. The patient's mother was also of Irish descent and died of pneumonia at the age of 87. Neither she nor her ancestry presented the Toher mark or other skeletal deformity. She had a fleshy tumor removed from the calf of the leg at middle age. The father had two brothers, both of whom presented the Toher mark. One had an elevation of one of his shoulders which was attributed to a bony tumor. The other's arms were limited in extension to about

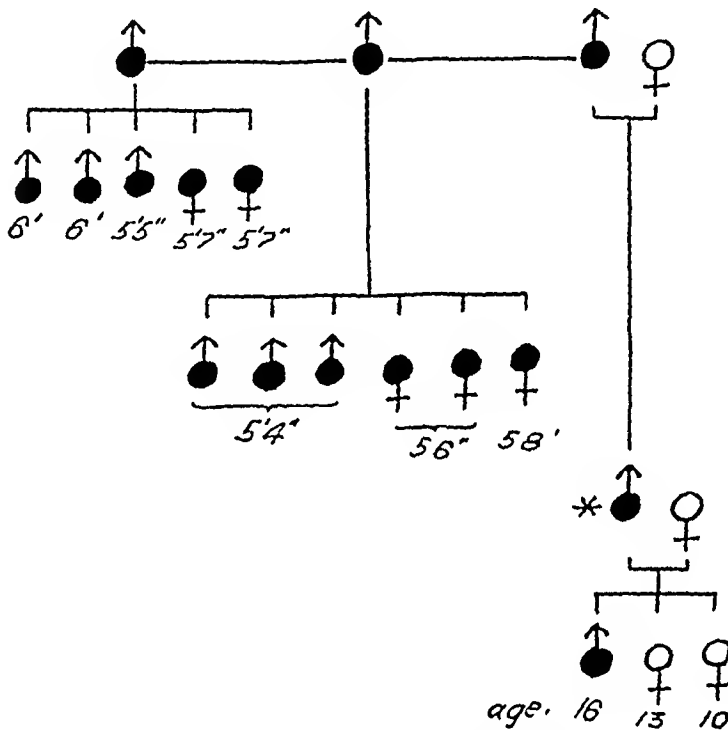


Fig 2—Family tree of Daniel T., showing hereditary and familial tendency of deforming chondrodysplasia. Affected persons are represented by the completely shaded circles, the unaffected persons by the unshaded circles. The asterisk denotes my patient.

45 degrees. One brother was the father of five children, three of whom were short in stature and two were 6 feet (183 cm) tall. One of the former was knock-kneed to such an extent that his legs were straightened by operation. All of the children, however, presented the Toher mark. The second brother had six children, all of whom showed this mark. The patient had three children, one boy and two girls. The boy was 16 years of age and was 5 feet, 9 inches (175 cm) tall, and although he did not present the Toher mark, a bony tumor had developed under the right knee since the onset of puberty. The girls were 13 and 10 years of age, and presented no visible deformities. A plan of the family tree is shown in figure 2.

The patient said that he had not had syphilis or gonorrhea. He did not use alcohol, but used tobacco freely. He had had the ordinary diseases of childhood and diphtheria, and he had had rheumatic fever and sciatica at the age of 10.

Three ribs were broken in 1910. He had had no other accidents and no operations. The cardiovascular, cardiorespiratory (except for frequent colds), the genito-urinary and the gastro-intestinal systems were normal. The nervous system was normal, except for the pathologic changes in the present illness.

The patient complained of multiple tumors over his body, which first attracted his attention at about the age of 14 and grew progressively as he grew. (He was born with the "Toher mark" but, to his knowledge, not with the enchondromas.) The tumors were not painful or tender until August, 1926, when the one at the right hip began to be tender and to enlarge rather rapidly. He began to



Fig. 3—Daniel T. (April 29, 1929). Note the limit of extension and deformity of the left forearm, tumors of the right hip and thigh and the lack of chondroplastic features of the cranium.

feel "sciatic pain" down to the foot in the region of the sciatic nerve. The foot grew somewhat numb and tingled, especially on the plantar surface. The toes became slightly bluish, and though the feet had always perspired a great deal, this one became dry. There were no other complaints.

After the first two roentgen treatments he said that all of the above phenomena disappeared, and the feet again became alike.

*Examination*—Physical examination showed the patient to be about 5 feet 6 inches (167.5 cm.) tall, well developed and well nourished, an intelligent, white

American man, appearing to be about 45 years of age. He came to the clinic on crutches, with an obvious flexion deformity of the right hip and markedly limited motion of the same. He did not appear to be in any pain and the physiognomy appeared normal.

The skin was warm and of normal thickness and consistency. There was a normal amount of moisture. No lesions were seen, and the growth of hair was normal for the male. The head was of normal shape and contour with a fair growth of slightly gray hair which was not unusual. The eyes were blue, and were not unusual. The ophthalmoscopic observations were negative.

The ears and nose presented no objective or subjective abnormalities. The teeth were in poor condition, and the tongue was rather deeply furrowed. The



Fig 4—Roentgenogram of the forearms of Daniel T (July 2, 1927). Note particularly the unfinished development of the distal end of the ulna and the enchondroma proximal to this. The attempt at pseudo-joint formation here has probably diverted the stimulus for epiphyseal growth.

tonsils were mildly hypertrophied, and the pharynx was mildly injected. There were a few small, soft and movable glands in the posterior triangles of the neck. The thyroid gland was not palpable, and there was no suggestion of stiffness of the neck.

The chest was symmetrical, well formed and of good and equal expansion. Litten's sign was present. The lungs were normal to percussion and auscultation. The point of maximum impulse of the heart was felt at the fifth intercostal space just inside the nipple line. It was not enlarged to percussion, and auscultation revealed no irregularities or murmurs. The pulse rate was 16 to the quarter, regular and of good volume and fair tension. The arterial walls were soft and elastic. The blood pressure was 110 systolic and 70 diastolic.

The abdomen was normal in appearance, being slightly rotund. There was no tenderness, fluid or masses to be felt. The solid organs were not felt.

The knee reflexes, ankle jerks and biceps, triceps and abdominal reflexes were equal and active on the two sides.

Both forearms and upper arms appeared shorter than normal. Both arms measured 28 cm. from the point of the shoulder to the external condyle of the humerus, and the forearms measured 21 cm. from the olecranon process to the region of the styloid process of the ulna. The left forearm was limited somewhat



Fig 5—Roentgenogram of the left humerus of Daniel T. (Oct. 2, 1927) showing exostosis in about the midshaft region.

in extension, as can be seen in figure 3, and the examiner at first thought that there was a congenital absence of the ulna. The upper third of the right humerus presented a nodular tumor fixed to bone and having the feel of an exostosis. The left humerus presented a similar tumor. The left lower extremity presented a similar tumor on the inner aspect of the lower third of the thigh. The right lower extremity presented a large tumor in this same relative location and a large tumor of the right hip. The latter tumor was a large symmetrical swelling which had eradicated the gluteal fold. The skin surface over it was slightly reddened and freely movable. The tumor was fairly well outlined and rounded. It was fixed securely to bone and was of bony consistency and smooth but there was a sense of fine irregularity. It was tender centrally to gentle pressure.



was the seat of the patient's pain. None of the other tumors was tender to even firm pressure. There was a fair degree of extension of the thigh, but flexion was quite limited. At the time of writing the circumference of the right hip was 72.5 cm compared with 58.5 cm of the left. The circumference of the right thigh in the region of the lower tumor was 55 cm compared with 50 cm on the left.

The laboratory examination was made on June 30, 1927. The blood count was hemoglobin, 75 per cent; red cells, 4,800,000; white cells, 6,550; differential count, polymorphonuclear neutrophils, 76 per cent; polymorphonuclear eosinophils, 3 per cent; small lymphocytes, 15 per cent; and endocytes, 6 per cent.

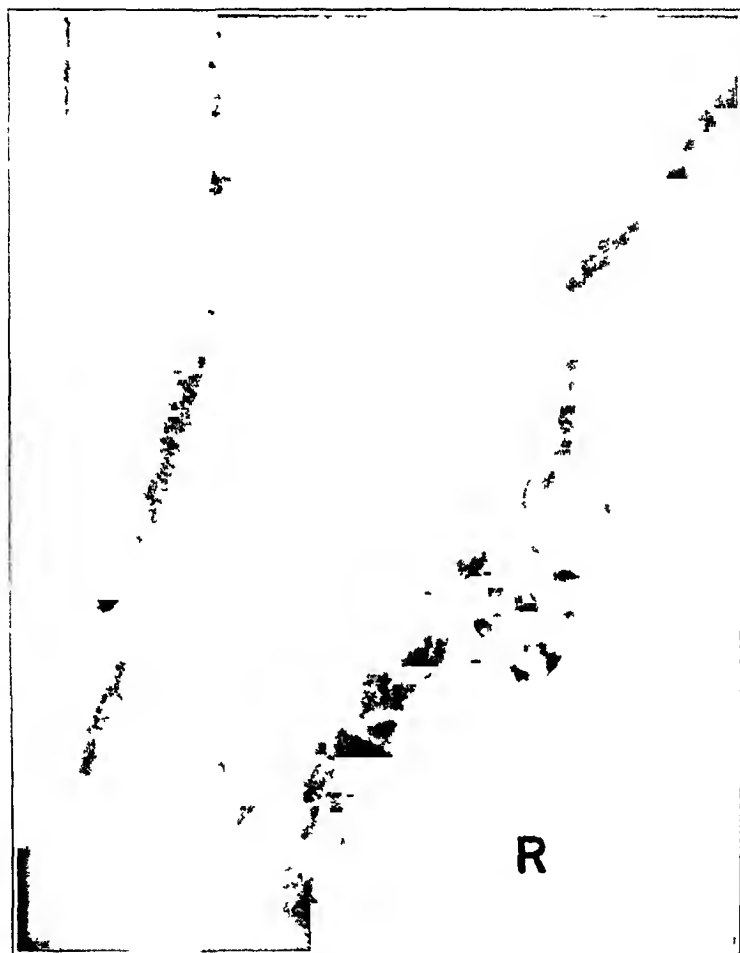


Fig. 6—Roentgenogram of the right femur of Daniel T. (April 4, 1929), showing large enchondroma in which chondromatous changes are beginning to take place comparable to those in the hip. Note also the small exostoses.

Urinalysis showed color amber; specific gravity, 1.030; albumin, 0; sugar, 0; acetone, 0; pus, blood, and casts, 0. The Bence-Jones test for protein was negative.

On April 29, 1929, the blood calcium was 14 mg. per hundred cubic centimeters.

Roentgenograms of the entire skeleton were taken, some of which are reproduced here. On June 30, 1927, Dr. T. F. Baxter reported a large osteoid type of bone tumor involving the region of the right hip at that time a benign tumor with none of the characteristics of sarcoma or carcinoma. There were also benign congenital osteoid tumors involving the lower shaft of the right femur,

upper portion of the right tibia upper portion of the left humerus distal portion of the left clavicle, upper portion of the right humerus chondral portions of the anterior regions of the ribs (more marked on the left side) both the right and the left radius and ulna (with deformity and widening of the shafts and marked deformity of both wrist joint areas and to a less extent of both elbow areas) lower portion of the shaft of the left femur upper portion of the shaft head and neck of the left and the right fibula and also of the right and the left tibia with evidence of a large pressure defect in the lower portion of the shaft and supra-condylar area of the left fibula

There was evidence of slight osteo-arthritis of the cervical spine and hypertrophic osteo-arthritis and some scoliosis of the dorsal and the lumbar spine



Fig 7—Roentgenogram (July 2 1927) of the legs of Daniel T. showing enchondromas. Note particularly the pseudo-joint formation at the distal end of the left tibia and fibula and the thinning out of the fibula beyond this joint.

*Course*—The patient returned to the hospital on September 27 at which time a check-up roentgenogram of the right hip was taken. The impression at this time was that the original osteochondroma had undergone malignant degeneration and exhibited the characteristics of osteochondrosarcoma. It was stated that it showed little or no evidence of extension since July 2 1927. There was evidence of a pathologic fracture through the neck of the right femur and of some reparative process in the tumor itself. From that time until the time of leaving the patient had returned every three months for roentgen therapy for what was considered an osteogenic sarcoma. The evidence of pathologic fracture had disappeared on April 25 1928. Similar changes were occurring in the tumor of the lower third of the right femur and by the same token had been regarded as malignant changes. The tumor of the hip had been growing steadily and rapidly and had been increasing markedly in its calcific content since July 2 1927.

laid down in multiple spots and in ringlike foci. Destruction of bone was not discernible in the most recent roentgenograms, those of the hip and the thigh being reproduced here.

At the time of writing the patient so far as his systemic condition was concerned, was enjoying excellent health. His appetite was good, and he said that he had recently gained some weight. The tumors of the hip and thigh in question, however, had obviously grown larger, and the former was somewhat tender in places to moderately deep pressure. The history concerning pain in the hip was not altogether clear, although he felt certain that it was alleviated considerably by the first roentgen treatment. It had been better and worse at intervals since and at the time of writing was so severe as to keep him awake a great part of the night.



Fig 8—Roentgenogram (July 2, 1927) of the right hip region of Daniel T., showing an osteochondroma. Note in all these pictures of the hip the absence of bone destruction and the ringlike manner in which the calcium is laid down in places.

The hip was completely fixed, and the skin over it was flushed and tightly stretched. Sensation of the extremity as compared with that of the opposite side appeared to remain normal, and both feet were of equal temperature, moisture and color.

The patient therefore presented marked and interesting changes which probably had taken place in one of the enchondromas and which merit some consideration as to their status between benignity and possible malignant changes. Cases of "malignant degeneration" of enchondromas have been reported in the older literature. These cases comprised about 5 per cent of all the cases of hereditary deforming chondrodysplasia that Ehrenfried was able to collect. Twenty-four

cases were reported in 1905 by Lenormant and Lecène.<sup>7</sup> The majority of these tumors reported by the older authors, however, are called chondromas or enchondromas, and the issue seems to have rested on the authors' opinion of the pathologic status of chondroma. In reference to all the literature reviewed so far, there seems to be no evidence except possibly in a single instance, that any of the malignant changes are other than chondromatous or osteochondromatous.<sup>8</sup> A few of the reports are accompanied by roentgenograms, and these bear out the foregoing statement. Dr Ehrenfried has felt, since the publication of his exhaustive study of hereditary deforming chondrodysplasia in 1917,

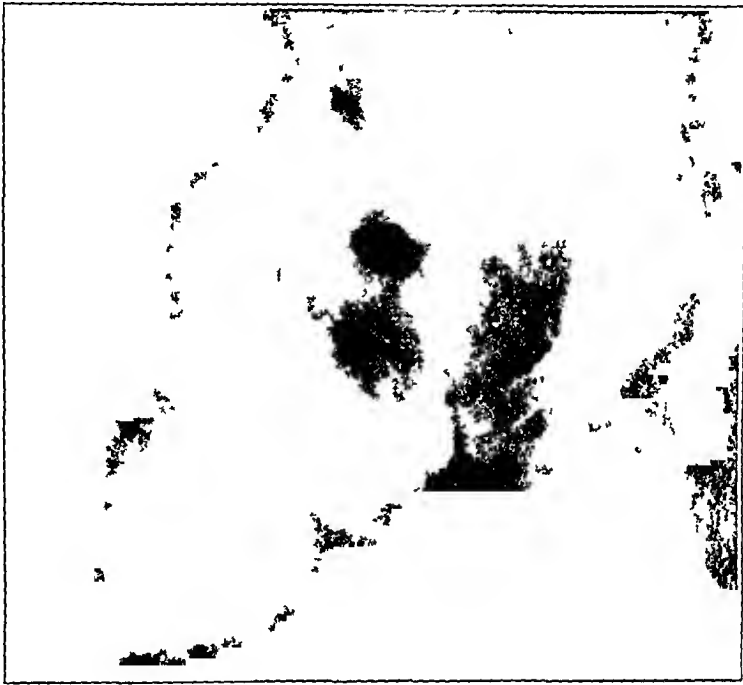


Fig 9—Roentgenogram (Oct 12, 1928) of the right hip of Daniel T. The apparent destruction of bone in the great trochanter here is due to a faulty roentgen exposure.

that instances of true malignant degeneration must be far more rare than he at first thought, and that there has probably been some confusion in making a differential diagnosis between hereditary deforming chondrodysplasia and chondromatosis. Bloodgood, in discussing Bogg's case, stated that there were no examples of malignant degeneration in multiple hereditary enchondromas and exostoses.

<sup>7</sup> Lenormant and Lecène. L'association des exostoses et d'un chondrome des os, *Rev d'orthop* 7 203 1906. Lenormant. Exostoses ostéogéniques et les chondromes des os. *Rev d'orthop* 6 193 1905.

<sup>8</sup> Dr Ehrenfried assisted me in obtaining these references.

The significant features of the tumor in the case reported here, which apparently arose from the proximal end of the right femur, are the relatively rapid growth and expansion, the extensive calcification or ossification, the absolute lack of visible evidence of bone destruction in the x-ray picture and over at least a three year period a systemic condition incompatible with malignancy. The x-ray picture shows that the calcium has been laid down in multiple foci and in ringlike structures, the latter pointing more strongly to a simple calcification in



Fig 10—Roentgenogram (April 26, 1929) of the right hip of Daniel T. Note the extension of the tumor medially and beyond the great trochanter.

the walls of degenerating cysts than to actual foci of ossification. I feel that such an observation in the x-ray picture characterizes this type of tumor. So far as I can ascertain, it is not found in osteogenic sarcoma, and such a design plus the absence of bone destruction can be taken as adequate evidence against that form of tumor.

In the following brief presentation of selected cases, a comparative study is made of the tumor in my patient and similar tumors reported in the literature. The latter have fallen into two classes: (1) those which illustrate a single and no doubt acquired chondroma in which

there are no hereditary features<sup>9</sup> and (2) those which are reported as being associated with multiple exostoses and which, though the hereditary factor of multiple exostoses and enchondromas is not stressed, are assumed to belong in the class of hereditary exostoses and enchondromas or hereditary deforming chondrodysplasia<sup>10</sup>

Paul Rostock<sup>11</sup> reported a case of chondroma of the hip which, although not of the hereditary type, will serve for comparison here. The two pictures have many points in common, and I believe it reasonable to suspect that the tumors are of essentially the same pathologic process. After an extensive study of his case, Rostock concluded that the tumor was a benign chondroma and in general that such tumors do not become malignant and are not initiated by trauma. These views are in accord with those of Lexer.

Lexer<sup>12</sup> reported a case of chondroma, the x-ray picture of which indicated the same fundamental pathologic changes as in the case in point. A colored drawing of the specimen in cross-section is also shown in his report.

Kienbock,<sup>13</sup> in a discussion of chondromas and sarcomas of bone, also showed x-ray pictures of ossifying chondromas which are excellent for comparison with the present case. He also regarded such tumors as benign.

Percy<sup>14</sup> reported a case of multiple chondro-osteoma in which a tumor was situated in the midregion of the right humerus. It increased in size rather rapidly, beginning its change at about puberty and enlarging from that of an orange to that of a coconut in three years. The x-ray picture of this tumor is shown in his report, but it is a picture slightly different from the one discussed here. In the tumor in

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9 Rostock, P. Die Unfallbegutachtung der Gelenkchondromatose, *Arch f Orthop* **26** 593, 1928. Lexer, E. Gelenkchondrome, *Deutsche Ztschr f Chir* **88** 311, 1907. Kienbock, R. Ueber Gelenkkopfschondrome und Sarkome, *Fortschr a d Geb d Rontgenstrahlen* **24** 468, 1917.

10 Percy, N. M. Multiple Chondro-Osteoma, *Surg Gynec Obst* **20** 619, 1915. Gangolphe, M., and Gabourd, J. Enorme enchondrome costal chez un sujet exostotique, *Rev d'orthop* **8** 201, 1907. Weber, O. Zur Geschichte des Enchondromes namentlich in Bezug auf dessen hereditares Vorkommen und secundäre Verbreitung in inneren Organen durch Embolie, *Arch f path Anat u Physiol* **35** 501, 1866. Haberer, V. Ein Fall von multiplen Enchondromen und Exostosen, *Arch f klin Chir* **89** 782, 1909. Stark, H. Ueber Multiple Cartilaginäre Exostosen und deren klinische Bedeutung, *Beitr z klin Chir* **34** 508, 1902. Liwen, A. Ueber die Beziehungen der Enchondrome zu den multiplen cartilaginösen Exostosen, *Deutsche Ztschr f Chir* **75** 14, 1904.

11 Rostock (footnote 9, first reference)

12 Lexer (footnote 9, second reference)

13 Kienbock (footnote 9, third reference)

14 Percy (footnote 10, first reference)

Percy's case the growth expanded in spicules and laminae rather than in the soap bubble and ringlike formations of the one in the patient whose case I have reported. Indeed one sees in his picture a sunburst effect which itself is not unlike that in osteogenic sarcoma, but there is no evidence of bone destruction. The report is of special value as the tumor was removed and the pathologic changes were reported.

The pathologic report was given as follows:

*Gross*—The tumor is hard and cauliflower-like in appearance. It measures 13.5 cm by 12.5 cm in diameter. The surface of the whole tumor is covered with a layer of glistening cartilage 3-6 mm in thickness. Beneath the cartilage is a mixture of bony and cartilaginous substance about 1 cm thick. The remainder of the tumor consists of a framework of hard bony material with many spaces resembling the medullary cavity of bone.

*Microscopic*—The outer layer is all cartilage but just internal to it are deposits of calcium in the matrix of the cartilage. Deeper in the tumor the calcium deposits take on more of the appearance of bone in the shape of lamellae interspaced with dense cellular tissue resembling blood elements.

*Pathological Diagnosis*—Osteoid chondroma.

Gangolphe and Gabourd<sup>15</sup> demonstrated a very large chondroma of the ribs which they incompletely resected, and which in its continued growth into the chest was fatal. The patient presented other exostoses. It may be observed that these rapidly growing chondromas are located practically always in or about joints, but that the exostoses are not infrequently at various distances from the joints. These authors quoted and endorsed Virchow in his belief that difference in vascularity has much to do with these two types of growth. They recognized the innocent benignity of the exostoses and advised no surgical attack unless there was unwonted encroachment on vital structures. On the other hand, they regarded the chondroma as malignant and advised its early and complete removal.

Weber<sup>16</sup> presented a case of multiple exostoses in which a very large, rapidly growing chondroma of the hip joint metastasized to the iliac veins and vessels of the lungs.

Haberer<sup>17</sup> demonstrated the case of a middle-aged man with multiple exostoses and enchondromas who showed large, rapidly growing chondromas of the left hip, distal end of the right femur, proximal end of the right tibia and the right calcaneus. X-ray pictures of this case are reproduced in his article and are comparable with mine.

Stark<sup>18</sup> presented a case of multiple exostoses, in one of which (on the right humerus) a malignant degeneration occurred. He quoted Chiari as believing that the condition originated from the marrow and

15 Gangolphe and Gabourd (footnote 10, second reference)

16 Weber (footnote 10, third reference)

17 Haberer (footnote 10, fourth reference)

18 Stark (footnote 10, fifth reference)

that the exostosis was probably responsible. Stark is of the opinion that such exostoses, which have practically the same structure and composition as normal bone, are only the coincidental location of a malignant condition, and that this is no more unusual than a sarcoma in normal bone. The author stated that this is the only case of a malignant change in an exostotic tumor that has been reported.

Lawen<sup>19</sup> presented a case of multiple cartilaginous exostoses. One of the tumors, involving the right scapula, part of the humerus and part of the clavicle, grew to be almost as large as the patient's chest. In his study of the case as to differentiation between malignant degeneration and chondroma, the former was ruled out, since the tumor had existed for about four years without apparent metastasis and since the patient was otherwise well.

Lenormant and Lecene studied rather closely the association of multiple exostoses and chondroma in the same patient and presented a number of case reports. They concluded that chondromas or osteochondromas may develop by superimposition on a previously existing exostosis or enchondroma, or that they may develop in a subject having multiple exostoses and enchondromas but independent of those lesions.

It will be observed that while part of the time I have been discussing the nonhereditary form of chondroma and part of the time a type of chondroma that has developed in a patient presenting multiple exostoses and enchondromas, there is adequate reason to believe that the two tumors are pathologically identical, that is, they are chondromas or osteochondromas. The terms chondroma and osteochondroma are used synonymously here since the degree of ossification does not alter the fundamental nature of the tumor. It must not be forgotten, also, that multiple exostoses and enchondromas are synonymous with hereditary deforming chondrodysplasia.

Thus it is at once obvious that a difference of opinion exists as to the pathologic status of chondroma. I think it can be conceded, however, that the consensus is against its being malignant in the accepted sense of the term.

#### COMMENT

It will probably be of value here to give a brief resume of the pathology of chondroid tumors, much of which is taken from Ewing.

Limited outgrowths of preexisting cartilage occur on the ribs, in the larynx and about the joints, which exhibit the characters of simple hyperplastic processes and are called ecchondroses. True progressive neoplasms composed of cartilage appear in the same situations and also in tissues not normally containing cartilage, and these are called chondromas or enchondromas.

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<sup>19</sup> Lawen (footnote 10 sixth reference)



It has long been recognized that chondromas have the property of rapid growth and may invade vessels and extend a long distance in them. They may grow into vessels and metastasize. Metastases are formed especially in the lungs. They have been known to invade the veins of the pelvis and extend to the heart. They undergo varying degrees of calcification and ossification. Ranvier has classified them in four groups according to their structure: (1) a single lobe of hyaline cartilage, (2) several lobes of hyaline cartilage separated by fibrocartilage, (3) fetal cartilage and (4) cartilage with stellate cells. Grossly, the tumors vary in consistency, some being soft and apparently more cellular than others. They undergo varying degrees of cystic degeneration and may ulcerate through the skin. It is likely that the vessel-invasive and metastasizing propensities depend on the nature of the tumor as outlined. The metastatic lesions are most frequently found in the pulmonary vessels, and this fact bears witness that the metastatic lesion is a vascular embolic one, probably having broken from a part of the tumor invading a vein. As is frequently true of metastatic thyroid tumors, a cross-section of the metastasis cannot be distinguished from the normal tissue of the new growth; in this case, normal cartilage.

A definitely malignant tumor (chondrosarcoma) is much more rare and differs from the foregoing in having definite infiltrative properties and being destructive of bone.

The chondroma, therefore, while having the property of invading vessels and truly metastasizing, is not malignant in the same sense and certainly not in the same degree as osteogenic sarcoma, and herein lies the tremendous difference in prognostic attribute. The chondroma strikingly lacks the debilitating and toxic influence of sarcoma of the bone. If a chondroma is inclined to metastasize, it undoubtedly does so late. If only a portion of the tumor is removed, the remainder will of course continue to grow, but if the gross tumor is completely excised, it will not recur. The indication therefore seems clear. A chondroma, whether it is of the nonhereditary type or whether it has developed on a skeleton presenting hereditary deforming chondrodysplasia, should be immediately totally excised so far as it is technically possible. It is doubtful whether roentgen therapy is of any benefit; it certainly is not curative.

In the case that I have reported, it is hardly possible to tell whether the osteochondroma developed secondarily on a preexisting lesion or whether it developed independently, and in the light of the present study, it would seem to me that such knowledge would at most be of only academic interest. I would add, however, that the association of osteochondroma with hereditary deforming chondrodysplasia is altogether too frequent to be regarded as merely coincidental. It would seem that the latter disease, either by virtue of its own etiology or by

the disruption of the cartilage at the epiphysis has especially predisposed its victim to chondromatosis. These patients, therefore, should be followed up carefully from time to time so that any newly developing chondroma may be totally excised in its infancy.

#### CHONDRODYSPLASIA AND CHONDRODYSTROPHIA FETALIS

In groping for a classification of hereditary deforming chondrodysplasia and a fitting category in which to place it in the list of skeletal deformities, particularly among those of congenital and hereditary nature, authors have permitted themselves to see a close kinship to achondroplasia or chondrodystrophia fetalis. They have been impressed by the abnormal shortness of limb and often of stature of these patients, making their bodies, exclusive of the head, appear not altogether unlike the chondrodystrophic dwarf. This, together with the fact that the condition is primarily a disturbance in epiphyseal growth, has been, I think, the chief influencing factor.

Among those who have made statements regarding a comparison of the two diseases are Lewin<sup>20</sup> and Dwyer,<sup>21</sup> who maintain that there is a close kinship, and Carman and Fisher,<sup>22</sup> who are of the opposite opinion.

Dwyer based his comparison on the following facts: 1. Achondroplasia, according to Kaufman, may be present without dwarfing and with widely varying degrees of involvement. 2. Both conditions affect only those bones that develop from cartilage. 3. Aberrant cartilage inclusions may be found in bones in both conditions. 4. There is a similarity in the pathology of the epiphyseal line, in that both conditions cause a chaotic appearance of the epiphyseal cartilage at the line of ossification.

Although it is true that both diseases are manifestations of a disturbance in epiphyseal ossification and a distortion of the rows of cartilage cells—a distortion which may be either cause or effect—there are many fundamental differences between the two conditions to warrant a suspicion that the histologic resemblance is not conclusive, that is, although the seeds look alike, the mature plants bear considerable witness against their identity. Although it is true that there have been reported cases of incomplete chondrodystrophia, as in the two fetuses having involvement of the intracartilaginous bones of the head without interference with the growth of the long bones reported by

20 Lewin, P. Multiple Cartilaginous Exostoses—Diaphyseal Aclasis, *Surg Gynec Obst* **45** 48, 1927.

21 Dwyer, H. L. Chondrodysplasia. Multiple Cartilaginous Exostoses, *Am J Dis Child* **19** 189 (March) 1920.

22 Carman and Fisher. *Ann Surg* **61** 142, 1915.

Kaufman, to all general intents and purposes true chondrodystrophia is a generalized disease. All of the epiphyses usually share the disorder equally, thus giving a generalized and symmetrical skeletal deformity. Again, while Schott described a type of chondrodystrophia appearing at puberty, to which he gave the name chondrodystrophia adolescentium, the majority of chondrodystrophic persons either are born prematurely or are dead at term (Nathan<sup>23</sup>). Chondrodystrophia is therefore in the majority of instances a serious fetal disease and indeed an antenatal disease, whereas chondrodysplasia is usually postnatal in its development and manifestation, and fatality has scarcely deserved consideration except as attributed to distinctly secondary causes.

One of the most characteristic features of chondrodystrophia is the unmistakable appearance of the physiognomy. At birth the circumference of the head often equals the length of the body. As growth proceeds, the characteristic prognathous appearance and flattening of the nasal region result from a possible combination of several factors: premature synostosis and inhibition of the growth of the os tribasilare; shortening of the ethmoid and nasal bones with or without the foregoing; and a reduction in the angle formed by the basilar process of the occipital bone and the body of the sphenoid, the latter condition being called by Virchow kyphosis of the saddle angle. I have seen no report of a case of chondrodysplasia in which the patient presented the characteristic physiognomy of chondrodystrophia, and the photograph of the patient presented here exhibits no such feature.

Added to this, one often finds thick lips protruding, hypertrophied tongue and epicanthus, such features never to my knowledge having been described for chondrodysplasia.

Finally, the hereditary factor in chondrodystrophia is almost nil, as Nathan implied when he stated: "In one case a chondrodystrophic mother is said to have given birth to an infant similarly affected, but in all others we have nothing upon which to base a surmise as to the cause of this disease." For chondrodysplasia the facts are the contrary.

Nathan further stated that the female is somewhat predisposed in the former disease—his own cases were equally divided between the sexes—whereas in the latter condition males have distinctly predominated by three to one.

Therefore, although it is far from my intention to make a dogmatic statement, I feel that there is much to militate against the conception that the disease under discussion is an aberrant form of chondrodystrophia fetalis.

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23 Nathan, P. W. Chondrodystrophia Foetalis, *Am. J. M. Sc.* **127**: 690, 1904.

## CONCLUSIONS

1 The so-called malignant degenerative lesions in skeletons presenting hereditary deforming chondrodysplasia are probably all chondromatous

2 A chondroma developing in a skeleton showing hereditary deforming chondrodysplasia is essentially the same pathologic process as the nonhereditary chondroma and should be regarded in the same light

3 Although such chondromas are essentially benign, they should, in view of their vessel invading and metastasizing propensities and rapid expansive growth, be totally excised as early as possible. Therefore, it is incumbent on the surgeon to make a check-up examination at intervals when he has diagnosed hereditary deforming chondrodysplasia

4 Roentgenotherapy probably has no beneficial effect on this type of tumor

5 The definite ringlike foci in which the calcium is deposited in the tumors, particularly in the absence of bone destruction, is adequate evidence on which to make a diagnosis of osteochondroma

6 The marked deformity and foreshortening of either or both of two juxtaposed bones in hereditary deforming chondrodysplasia is probably due to pseudo-joint formation and distorted stimulus of bone growth

7 There are so many factors militating against a possible kinship of chondrodystrophia fetalis and hereditary deforming chondrodysplasia that one would as yet seem unjustified in placing them in the same category

# SYNDACTYLISM

(COHERENCE OF THE FINGERS OR TOES)\*

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The interest of surgeons in webbing of the fingers and toes is evidenced by the numerous contributions that have appeared in the literature during the last century and a quarter. Our own interest was stimulated by the care of a considerable number of these patients and by the fact that there still seemed to be much confusion about the subject. An attempt will be made in this paper to clarify the matter by tracing the deformity from its origin to its correction by the methods that have been most satisfactory in our hands.

## DEFINITION

*Congenital Syndactylism*—This type is an inheritable developmental defect characterized by complete or partial webbing of the fingers or toes. This malformation varies greatly in degree, from a slight distal extension of the normal web to complete fusion extending to the ends of the fingers.

*Acquired Syndactylism*—Although usually a congenital malformation, syndactylism may be acquired and not infrequently follows severe burns or trauma of the hands or feet in which destruction of the tissues of the fingers or toes results in subsequent fusion of granulating surfaces.

The term "syndactylism" has been erroneously used in the literature to designate partial or complete lack of toes or fingers, but this type of defect is due to deep developmental disturbances while the webbing of the fingers or toes is merely indicative of an arrest in otherwise normal development. The cause of this arrest of development is as yet unknown.

## CLASSIFICATION

Syndactylism may be classified according to the degree of fusion, as complete when it extends to the tips of the digits, and incomplete

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\* Submitted for publication, Nov. 9, 1929.

\* From the Surgical Department of the Johns Hopkins University and Hospital, Division of Plastic Surgery.

when the fusion is of a lesser degree. When the phalangeal bones are normal, the type is simple. When they are abnormal in size, shape, number and arrangement, the type is complicated.

The simplest type is that in which the web consists of the skin only, and this may be slack enough to allow the fingers to be separated to a considerable distance. More commonly the skin and underlying soft parts are involved, the fusion often extending to the ends of the fingers. Frequently there is only a shallow groove on each side to indicate the line of normal division. Sometimes the fingers may be even more closely fused, the nails being joined, and in extreme cases the phalangeal bones also. The terminal phalangeal bones are those most frequently fused.

In certain types of syndactylism in which the web is thin, lax and short, there is little interference with function, except that the fingers cannot be widely separated. On the other hand, when the fusion is close, there is complete loss of individual digital function, and the fused fingers must necessarily be flexed and extended as one. This is frequently a serious handicap, and relief can be obtained only by surgical procedure.

In the acquired type, the web generally consists of dense scar tissue, and there is usually an associated contracture or distortion of the digits, but there is seldom, if ever, fusion of the bones. The acquired type may also be complete, but in the majority of instances the fusion is incomplete.

#### EMBRYOLOGY

The embryology of the extremities has been studied by Bardeen and Lewis<sup>1</sup> and by Lewis<sup>2</sup>. In the development of the embryo, the arm bud makes its appearance during the third week as a swelling in the lower cervical region. At this stage there is no differentiation of the mesenchyme, although a few thin walled blood vessels are present.

The condition of the hand at 4½ weeks is shown in figure 1. The border vein is present, but there is no evidence of differentiation in the hand plate.

During the fifth week, the hand plate shows several centers of increased condensation corresponding to the carpal bones. From the carpus, five masses of condensed tissue project, these are the finger masses. This stage is shown in figure 2.

By the sixth week, the metacarpals and phalanges have appeared as distinct masses of cartilage. No joint cavities are present but the

1 Bardeen, C. R., and Lewis, W. H. Development of the Back Body Wall and Limbs in Man. *Am J Anat* 11, 1901.

2 Lewis, W. H. The Development of the Arm in Man. *Am J Anat* 11, 145, 1901.

cartilages are separated by areas of condensed tissue. The intrinsic muscles of the hand are represented by late pre-muscle tissue and a few muscle fibers.

During the seventh week, the development of the metacarpals and phalanges proceeds rapidly, and the ligaments appear. There is now a definite commissure between the fingers, although considerable webbing remains at their base. All the muscles are present and are composed of muscle fibers. Figure 3 illustrates this stage. Ossification of the metacarpals and phalanges begins in from the seventh to the twelfth week. The interdigital commissure rapidly deepens after this period.

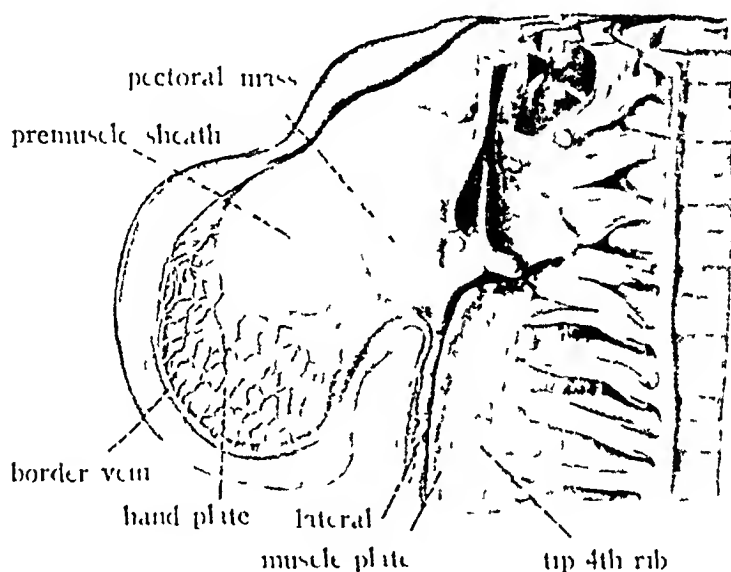


Fig. 1—Hand plate in a 4½ weeks' embryo (Lewis). The border vein is present, but there is no evidence of differentiation in the hand plate.

The foot is developed in a manner similar to that of the hand. The posterior limb bud appears during the third week as a projection from the wolffian ridge opposite the twenty-first to the twenty-sixth spinal segments. In general, the development of the structures of the posterior limb occurs about one week later than that of the corresponding parts of the arm. Most of the main structures of the posterior limb may be distinguished by the end of the seventh week.

#### COMPARATIVE ANATOMY

Straus<sup>3</sup> recently reviewed this phase of the subject and described syndactylism occurring in the primates, the insectivores, the rodents and

<sup>3</sup> Straus, W. L. The Nature and Inheritance of Webbed-Toes in Man. *J. Morphol. & Physiol.* 41: 427, 1925.

the primitive marsupials Beddard<sup>4</sup> stated that in the last group mentioned, all of the family *Macropodidae*, including the kangaroo, normally have the second and third toes united by a web. Among the rodents, many of the aquatic forms, including the beaver, have toes completely or partially webbed. Many of the aquatic forms of insectivores, including the moles, have the toes normally united by a web. Among the more common primates, *Catarrhinae*, or Old World monkeys, shows the normal presence of webbing between the fingers and toes in the genus *Cercocebus*. The siamangs of Sumatra and the Malay

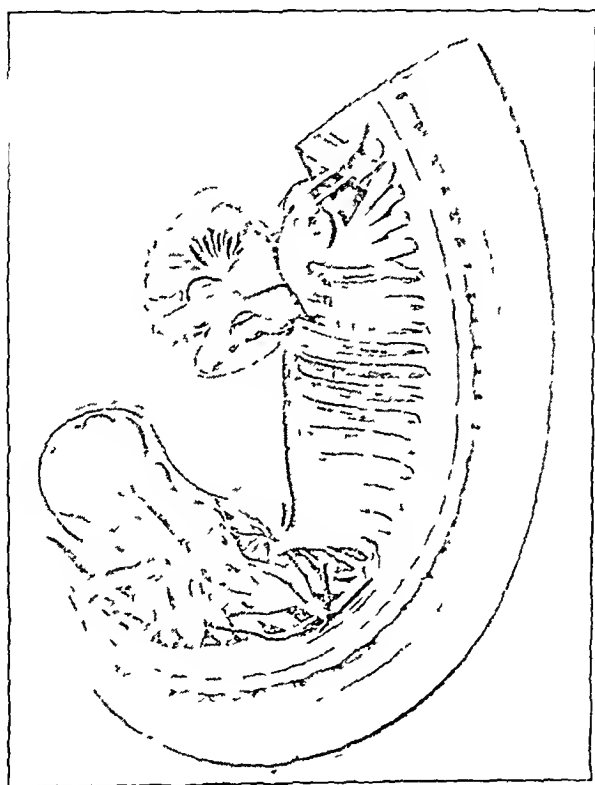


FIG 2—The hand and foot in a 5 weeks' embryo (Bardeen and Lewis). From the carpus five masses of condensed tissue project, which are the finger masses. Centers of increased condensation corresponding to the carpal bones are also present.

Peninsula normally have a web between the second and third toes, as shown in figure 4. Syndactylism has also been described occasionally in the orang-utan, the gorilla and the chimpanzee. In the insectivores and the rodents, this condition may be regarded as an adaptation to an aquatic form of life. In some forms of the primates, as suggested

<sup>4</sup> Beddard, F. E. *Mammalia*, in *Cambridge Natural History*, New York, The Macmillan Company, 1902, vol. 10.



by Weidenreich,<sup>5</sup> this persistence of webbing may be an adaption to an arboreal existence

#### PATHOLOGY

The deformities of the hand have been classified by Nichols<sup>6</sup> under three heads (1) those depending on deficient development, achennia (absence of the hand), ectrodactylism (absence of one or more digits) hypophalangism (absence of one or more phalanges), (2) excessive development polychennia, polydactylism, polyphalangism (3) perverted

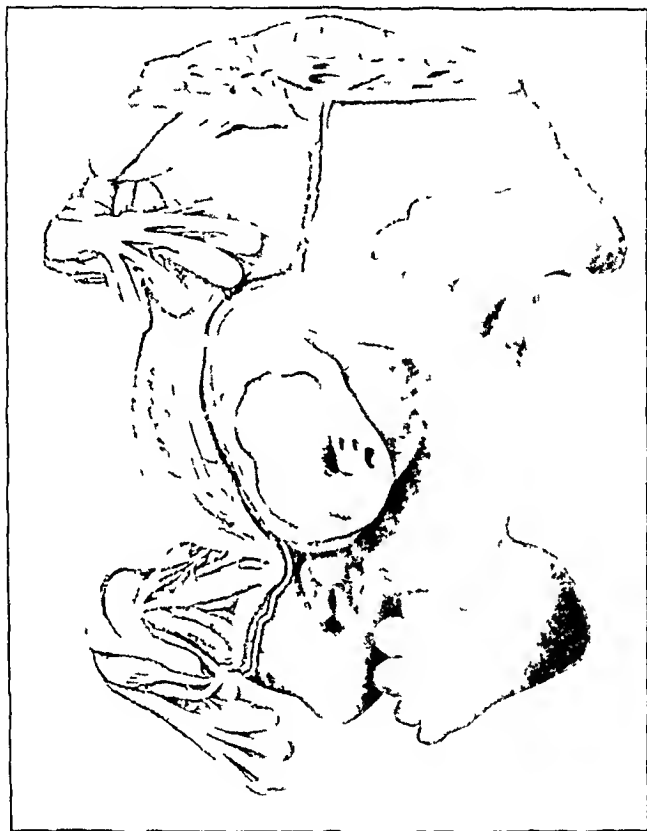


Fig 3—The hand and foot in a 7 weeks' embryo (Bardeen and Lewis) Development of the metacarpals and phalanges proceeds rapidly and ossification begins from the seventh to the twelfth week. The ligaments have appeared. There is a definite commissure between the fingers which deepens rapidly from this period. The development of the foot proceeds in a similar manner, but in general is about one week later than that of the corresponding part of the hand.

development, syndactylism, cleft hand, congenital constrictions, congenital dislocations, congenital neoplasms. From this classification, it will be noted that syndactylism may be considered merely a local arrest of normal development.

<sup>5</sup> Weidenreich, F. Der Menschenfuss, Ztschr. f. Morphol. u. Anthrop. **22** 51, 1922.

<sup>6</sup> Nichols, E. H. Reference Handbook of Medical Sciences, New York, Buck, 1902, vol. 4.

In the congenital cases, in addition to the syndactylism, there may be malformation of the bones of the hands or feet. Lepoutre<sup>7</sup> reported an unusual case of this type with syndactylism and marked deformity of the bones of the hands and feet in a mother and her child. The child also showed an unusual forking of the tips of several fingers. Clark<sup>8</sup> reported a case of bilateral syndactylism of the two ulnar digits, with absence of the radial digits. The same condition was found in the patient's father and her two brothers. The patient in the case reported by Epstein,<sup>9</sup> with no family history of syndactylism, had a cleft right hand, with complete absence of the middle phalanx, and the other



Fig. 4—Normal syndactylism in the foot of a Siamang ape (redrawn from Schultz). Note the partial fusion of the second and third toes.

fingers were webbed. The feet were cleft and the toes webbed, but the left hand was normal. Groves<sup>10</sup> reported a case of syndactylism in which the proximal phalanx of the middle finger was in a transverse position and attached to the second finger.

7 Lepoutre. Malformations congenitales des extremités chez un enfant et chez sa mère, *Rev. d'orthop.* **10** 237 1923.

8 Clark, W. E. LeG. A Case of Hereditary Syndactylism, *Lancet* **2** 434 1916.

9 Epstein, J. Perodactylism, Syndactylism and Cleft Extremities in a Child, *New York M. J.* **9** 153 1919.

10 Groves, E. W. H. An Unusual Case of Syndactylism, *Brit. J. Surg.* **1** 143, 1913.

A case similar to that reported by Groves was found in our series. In this instance there was bilateral webbing of the fourth and fifth fingers with fusion of the terminal phalanges. Another patient with bilateral webbing of the third and fourth fingers showed fusion of the terminal phalanges on the right with bilateral duplication of the terminal phalanges of the fourth finger, the duplicated phalanges being fused at each end. In another case illustrating the association of bony deformity with syndactylism, there was locking of the phalanges of the fourth finger of one hand and deformity of the same bones of the other hand.

Cases of syndactylism, associated with intra-uterine partial amputation of the fingers or toes, have been reported by Assali,<sup>11</sup> Deeg,<sup>12</sup> and Coleman.<sup>13</sup> These deformities were attributed by Deeg and Ehringhaus<sup>14</sup> to the presence of amniotic bands. These bands, however, have never actually been demonstrated. In more than 8,000 specimens entered in the Carnegie Embryological collection Streeter<sup>15</sup> found eight fetuses demonstrating various stages of the phenomenon of intra-uterine amputation. There was no evidence in any of these of amniotic bands or adhesions. Occasionally, in macerated fetuses, rolls of macerated epithelium were found giving the appearance of constricting bands. Streeter, however, expressed the belief that neither the epithelial rolls nor the umbilical cord can account for the constrictions. Instead, he found localized areas of necrosis affecting the amputations, either by complete destruction of the part or by forming an annular area sufficiently extensive to cause the sloughing off of everything peripheral to it. In the process of necrosis there is a tendency toward the formation of strands of fibrous tissue which may give the appearance of constricting bands. These are not, however, the primary cause of amputation, and they are not amniotic in origin. The active period of the tissue necrosis was found in the fetuses of from 12 to 20 weeks, in the second half of pregnancy, the process was found either as a completed amputation or in the stage of arrest with more or less complete healing of the area affected.

Daraignez, Masse and Subervie<sup>16</sup> reported a case of syndactylism

11 Assali, J. Amputations digitales, syndactylie, extrodactylie et sillons congénitaux, déterminés par brides amniotique, *J de med de Bordeaux* **51** 107, 1921.

12 Deeg. Zwei selten Fälle von angeborenen Missbildungen, *Beitr z klin Chir* **126** 429, 1922.

13 Coleman, H. A. Coexistence of Congenital Amputations and Syndactylism, *J A M A* **83** 1164 (Oct 11) 1924.

14 Ehringhaus, O. Zur Pathologie und Therapie der Syndactylie, *Berl klin Wchnschr* **49** 421, 1912.

15 Streeter, G. L. Personal communication to the authors.

16 Daraignez, Masse, L., and Subervie. Syndactylie et polydactylie, *J de méd de Bordeaux* **54** 363, 1924.

of one hand and both feet, with polydactylism of the feet. Syndactylism was present in the paternal grandfather, a brother and a child of the patient. In a similar case in our series, the patient had webbing of the third and fourth fingers of one hand and polydactylism of both hands and feet.

The association of syndactylism with acrocephaly has been reported in about forty cases. The cases up to 1926 were reviewed by de Bruin<sup>17</sup> who found that the prognosis as to life was favorable, but that vision was frequently threatened. Only two of the patients were idiots, the remainder apparently being normal mentally. There is a huge, round protruding skull above the level of the eyes, and exophthalmos is usually present. Most of the patients show no familial or hereditary features, but Weech<sup>18</sup> recently reported a case with almost identical deformity of the head, hands and feet occurring in a mother of 19 and her daughter of 11 months. It is probably due to a defect in the germ plasm, as in the case of simple syndactylism, rather than to externally operating causes. A case illustrating these associated deformities occurred in our series.

Dervaux,<sup>19</sup> reported an unusual case of syndactylism consisting of the union of the terminal portion of two adjacent fingers, which occurred in both hands. There was no fusion of the proximal ends of the fingers. One foot showed a similar deformity. There were no previous cases in the family history. There was a similar case in our series, with union of the distal ends of the second and fourth fingers of both hands over the top of the third finger.

#### INHERITABILITY

There are many cases in the literature and also in our series 18 per cent, illustrating the importance of an hereditary factor in syndactylism, and we feel that our percentage would have been higher had it been possible to obtain accurate data on this point. In the majority of cases, however, the family history was negative in this respect. Straus<sup>2</sup> studied the mode of inheritance as shown in a number of pedigrees assembled from the literature and from original cases and concluded that there appear to be four different hereditary groups.

In the first group, which appears to be the most common, the character is a mendelian dominant. This is illustrated in figure 5.

17 DeBruin, J. Acrocephalosyndactylism, *Nederl. tijdschr. v. geneesk.* **3** 2380, 1925, abstr. *J. A. M. A.* **86** 456 (Feb. 6) 1926.

18 Weech, A. A. Syndactylism and Acrocephaly, *Familial Bull. Johns Hopkins Hosp.* **40** 73, 1927, abstr. *J. A. M. A.* **88** 1677 (May 21) 1927.

19 Dervaux. Syndactylie terminale des mains et syndactylie d'un pied. *Bull. Soc. d'obst. de Paris* **12** 316 1909.

The example in the second group, figure 6 shows the character to be either a recessive in generation one for both parents, or to arise as a mutation in generation two, where it is a mendelian or sex-linked dominant

In group three the character is a mendelian or sex-linked recessive, figure 7. An example in our series also illustrates this type of inheritance, figure 8

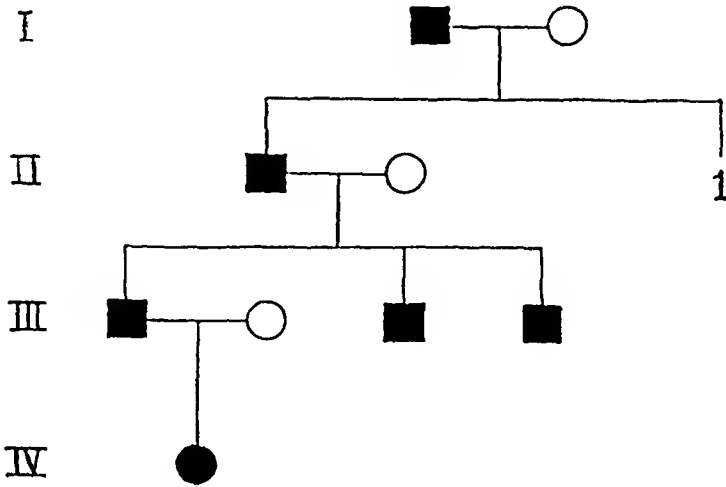


Fig 5—Pedigree showing syndactylism as a dominant mendelian character (Straus). The squares indicate males, the circles, females. The solid figures denote the presence of syndactylism, the open figures signify its absence. Each horizontal line represents one generation.

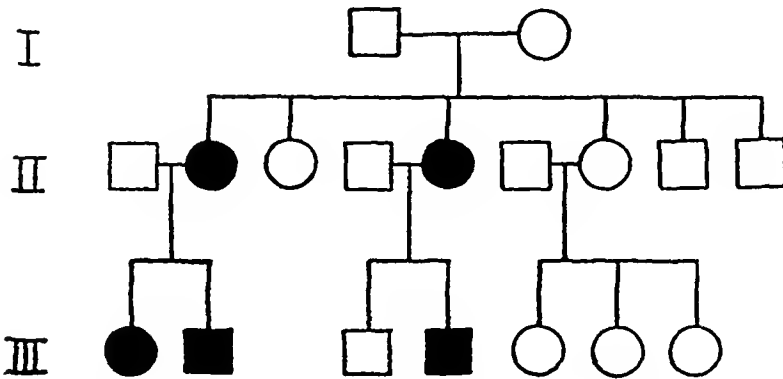


Fig 6—Pedigree showing syndactylism as a recessive, or arising as a mutation in generation II (Straus).

The fourth group consists of the case reported by Schofield,<sup>20</sup> in which the character of syndactylism is inherited by all the males of the family but never by the females, figure 9. It was pointed out by

<sup>20</sup> Schofield, R. Inheritance of Webbed-Toes, *J Hered* 12:400, 1921.

Castle<sup>21</sup> that this character follows the distribution of the Y chromosome. Schmidt<sup>22</sup> found a similar type of transmission of an exclusively male character in the fish *Lebistes reticulatus*. This coincides with Painter's<sup>23</sup> work indicating an X-Y sex-determining pair of chromosomes.

Straus<sup>3</sup> also reported a case of syndactylism occurring in one of a pair of otherwise identical twins.

From a study of the pedigrees of families with syndactylism, Schultz<sup>24</sup> concluded that the character apparently never skips a

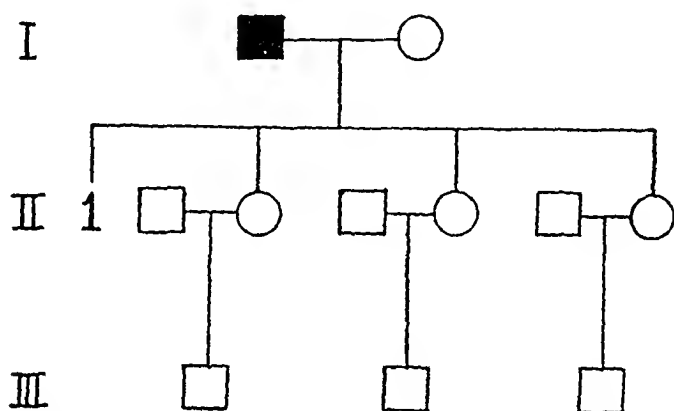


Fig 7—Pedigree showing syndactylism as a mendelian or sex-linked recessive (Straus)

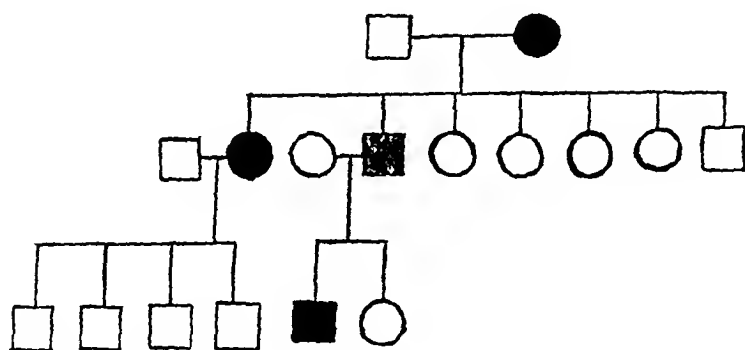


Fig 8—Pedigree of a case in our series, showing syndactylism as a recessive character

generation and the persons who are free from the condition will probably have normal children. It appears that the female is less likely to transmit the condition and is also less likely to inherit it.

21 Castle, W. E. Further Data on Webbed-Toes. *J. Hered.* **14**: 209, 1923.

22 Schmidt, quoted by Castle, W. E. A New Type of Inheritance. *Science* **53**: 339, 1921.

23 Painter, T. S. The Y-Chromosome in Mammals. *Science* **53**: 503, 1921.

24 Schultz, A. H. Zygodyctylia and its Inheritance. *J. Hered.* **13**: 113, 1922.

## INCIDENCE

The incidence of syndactylism has been studied by Schurmeier,<sup>25</sup> who found 8 cases among 20,000 men examined. An analysis of cases in the literature shows the condition to be more common in males, 63 per cent, compared to 37 per cent in females. In our 50 cases the ratio was 68 per cent males to 32 per cent females.

## SUMMARY OF CASES

Our series of 50 cases may be summarized as follows: males, 34 or 68 per cent, females, 16 or 32 per cent, color, white, 46 or 92 per cent, black, 4 or 8 per cent, family history of similar deformity, 9 or 18 per cent, no family history, 41 or 82 per cent.

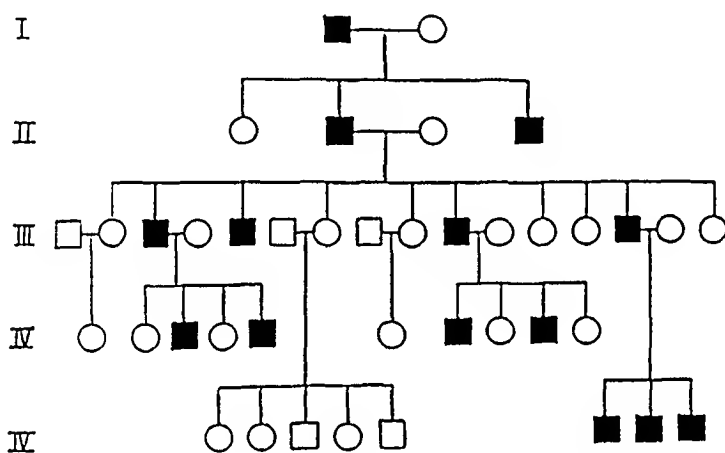


Fig. 9—Pedigree showing syndactylism as a sex-linked character (Straus)

For convenience we shall separate the cases into three general groups: Group 1, fusion of the fingers alone, Group 2, fusion of the toes alone, Group 3, fusion of the fingers and toes.

*Group 1*—Fingers alone, 30 cases, 60 per cent.

Second and third fingers: Right incomplete, 1, left complete, 1, left incomplete, 2, bilateral complete, 1.

Third and fourth fingers: Right complete, 3, left complete, 2, bilateral complete, 5, bilateral incomplete, 1, right incomplete, left complete, 1.

Second, third and fourth fingers: Left complete, 2, bilateral complete, 1.

Second, third, fourth, and fifth fingers: Bilateral complete, 1.

Third, fourth and fifth fingers: Bilateral complete, 1.

Fourth and fifth fingers: Left complete, 1, bilateral complete, 1.

<sup>25</sup> Schurmeier, H. L. Congenital Deformities in Drafted Men, *Am. J. Phys. Anthropol.* 5: 51, 1922.

First, second, third, fourth and fifth fingers Right complete, 1, left hand, first and second, also fourth and fifth, 1

First, second, also fourth and fifth fingers Left, incomplete, 1

Unsymmetrical bilateral fusions Right hand incomplete, second and third, left hand incomplete, fourth and fifth, 1

Right hand complete of stumps of the third and fourth, left hand complete, fourth and fifth, 1

Right hand complete, third and fourth, left hand incomplete, second and third, 1

Right hand, second to fourth over third, left hand, second to fourth over third, and fourth to fifth, 1

*Group 2*—Toes alone, 11 cases, 22 per cent

Second and third toes Right complete, 1, right incomplete, 2, left complete, 1, bilateral incomplete, 5

Third and fourth toes Bilateral incomplete, 1

Second, third, fourth and fifth toes Bilateral incomplete, 1

*Group 3*—Fingers and toes, 9 cases, 18 per cent

Bilateral complete, third and fourth fingers, bilateral incomplete, second and third toes, 1

Right hand complete, third and fourth fingers, left hand complete, third, fourth and fifth fingers, right foot incomplete, second and third, left foot complete, second and third toes, 1

Bilateral complete, second and third fingers, bilateral complete, second, third and fourth toes 1

Bilateral complete, second and third fingers, right foot, incomplete second and third toes, left foot complete, second and third toes, 1

Bilateral complete, second to fifth fingers, bilateral complete, first to fifth toes, 1

Right hand complete, third and fourth fingers, left hand incomplete second and third fingers, right foot complete, fourth and fifth toes 1

Left hand complete, third and fourth fingers, bilateral incomplete second and third toes, 1

Right hand incomplete, second and third fingers, left hand complete second and third fingers, right foot complete fourth and fifth toes 1

Right hand complete, fourth and fifth fingers, right foot incomplete, second and third toes, 1

*Concurrent Congenital Deformities*—In a case of complete fusion of the second and third fingers of the left hand, the fourth and fifth fingers with their metacarpal bones were missing

In a case of complete fusion of the second third and fourth fingers of the left hand there was arrested development of the entire hand and the middle phalangeal bones of the fused fingers were missing



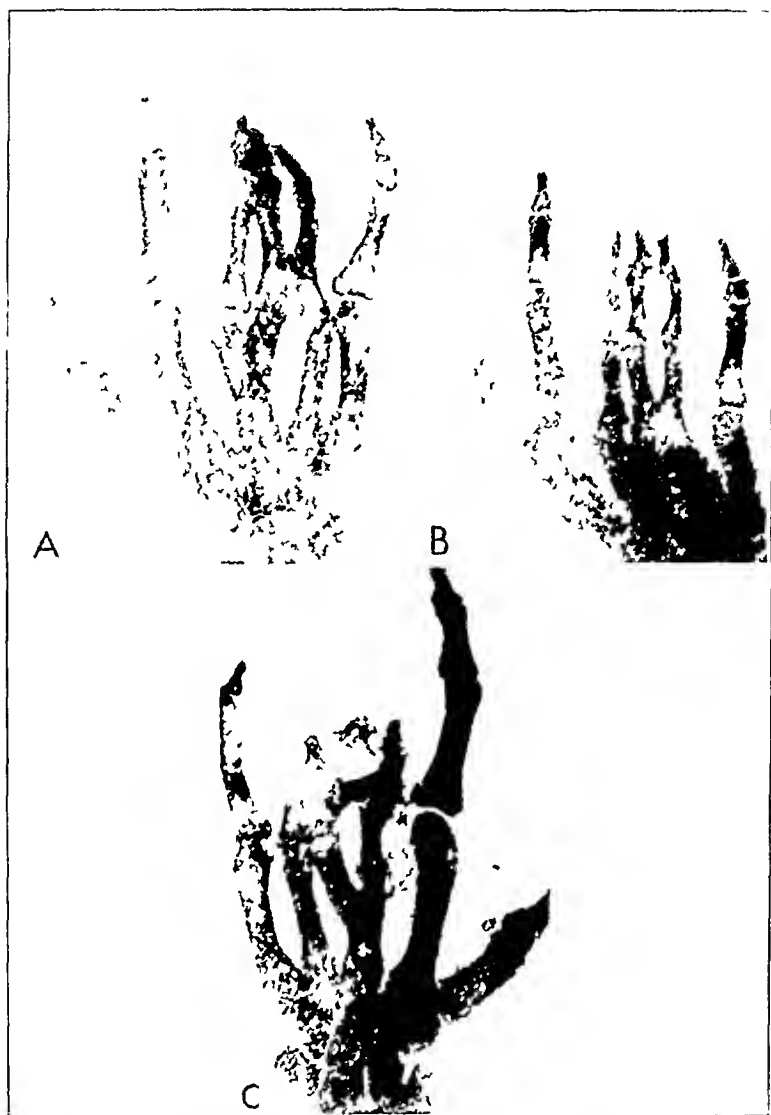


Fig 10—Bonnet and Treves' (Syndactylia and Polydactylia, Bull et mem Soc de chir de Paris 20 677, 1928) case, illustrating the inheritability of syndactylism. *A* and *B* show same hand, *C*, the other hand. The plates show the hands of a girl, aged 19, with a bilateral complicated type of syndactylism associated with polydactylism. The patient had two brothers and eight sisters. Three of the sisters presented the same malformation, as did all others in the family who were affected. The mother, the aunt and the female cousins had the same deformity, but the two maternal uncles were normal. From this it can be seen that in the last two generations only the women were affected, but in the preceding generation one finds the same malformation in the maternal grandfather, certain of his brothers and some cousins of both sexes. The patient said that she had been told that the same malformation had existed in the family for six or seven generations. A normal female child was subsequently born to the patient.

In a case of incomplete fusion of the second and third fingers of the left hand, there was arrested development of the entire hand and the second phalangeal bones of the fused fingers were much shortened

In a case of complete fusion of the thumb and all the fingers of the right hand, the middle phalangeal bones of the second, third fourth and fifth fingers were missing

In two cases of complete fusion of the second and third toes, one of the right foot and the other of the left, the second phalangeal bones were elongated and there was a tumor made up of small closely packed lobules of fat, involving the sole of the foot close to the root of the toes

In a case of bilateral fusion of the second and fourth fingers over the third there had been partial intra-uterine amputation of the third finger of the left hand and also of the terminal phalanges of the first and second toes of the right foot



Fig 11—Partial bilateral syndactylism of the complicated type. The hands of a girl, aged 3 years, with no family history of syndactylism. There had been partial bilateral syndactylism of the ring and middle fingers. Note the distortion of the fingers and the unusual development of bone. This child had been operated on several times before coming under our care and dense scar tissue increased the deformity and interfered with function. Excision of the scar, readjustment of the bones and grafting the denuded surfaces with whole thickness grafts considerably improved function. In this case the original operative work was done too early and the scar contracture markedly increased the lateral deformities.

In a case of bilateral fusion of the second to the fifth fingers and of all the toes, there was also acrocephaly and there had been intra-uterine amputation of the left thumb

In one case in which there was complete fusion of the third and fourth fingers of the right hand, there was a hydrocele

In one case, there was a hemangioma of the scalp

In one case with complete fusion of the stumps of the third and fourth fingers of the right hand and with complete fusion of the fourth and fifth fingers of the left hand the phalanges and metacarpals of the

first and second fingers, the phalanges of the third finger and the middle and terminal phalanges of the fourth finger of the right hand were missing. On the left hand, the phalanges and metacarpal bones of the first finger were missing, as were the phalanges of the second finger and all but the proximal portion of the proximal phalanx of the third finger. There were also bilateral crabclaw cleft feet, with the phalanges and metatarsals of the second, third and fourth toes missing.

In a case of incomplete fusion of the second and third toes of the right foot, there was a bifid thumb on the right hand.

In one case of bilateral fusion of the second, third and fourth fingers, there was also a bilateral talipes equinovarus and a deep con-

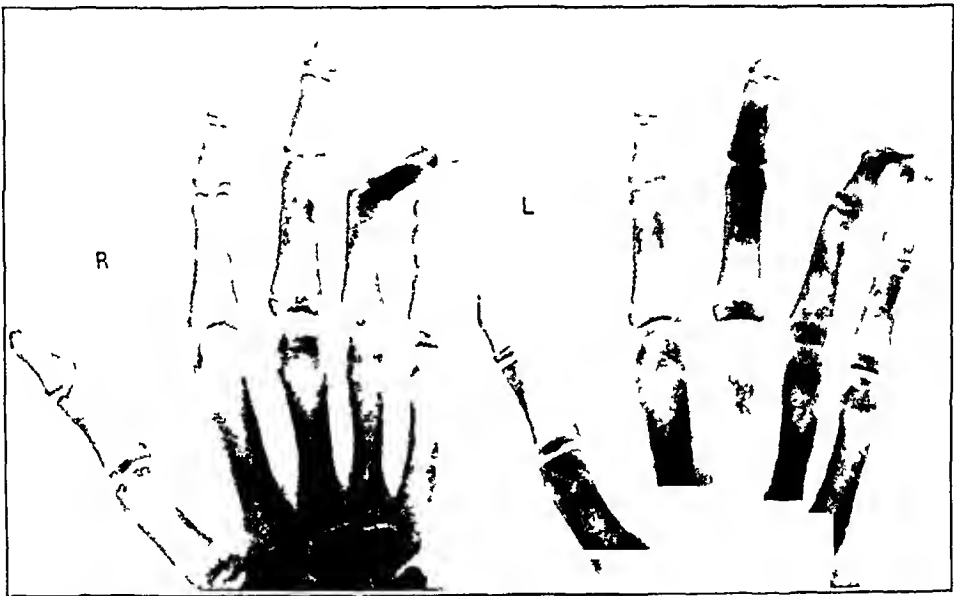


Fig. 12—Complete bilateral syndactylism of the complicated type. X-ray pictures of the hands of a boy, aged 17, with no family history of syndactylism. Note the unusual fusion and displacement of bone of the terminal phalanges of the ring and little fingers of both hands.

stricting band 0.5 cm. wide, around the lower third of the right leg above the ankle.

In a case of incomplete fusion of the second and third fingers of the right hand, there was also a large umbilical hernia.

In a case of incomplete fusion of the second and third fingers of the right hand and of the fourth and fifth fingers of the left hand, there was tongue-tie and an abnormality of the lower jaw, also bilateral talipes equinovarus.

In one case of complete fusion of the third and fourth fingers of the right hand, there was a congenital cleft of the palate and bilateral talipes equinovarus.

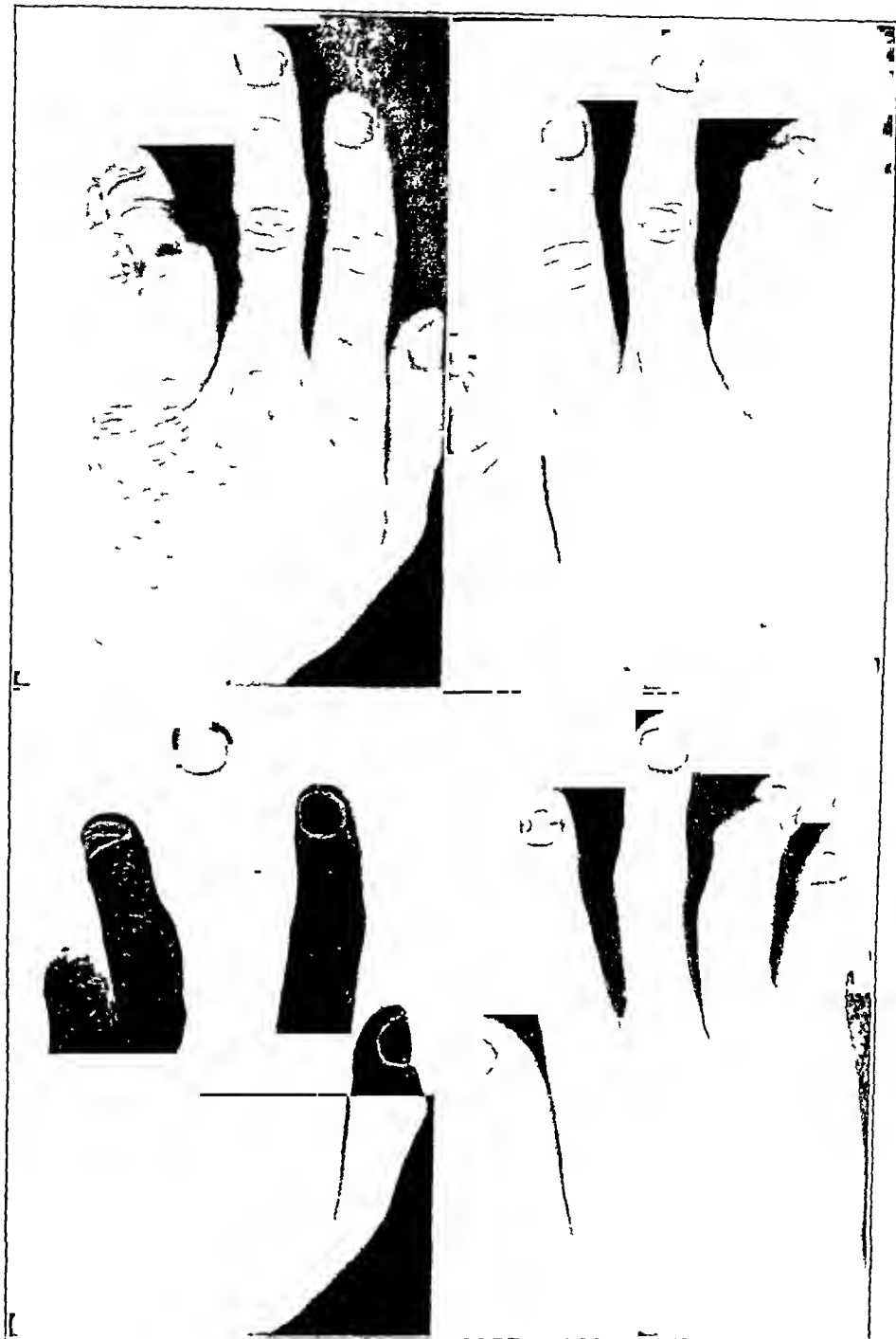


Fig 13—Photographs of the hands shown in figure 12. The bilateral fusion of the fingers can be well seen. The marked distortion of the fused fingers is probably due to the long period during which the condition has been allowed to remain unrelieved and illustrates the importance of the early separation of fused fingers of unequal length so that each finger may be unrestricted in its growth. Without doubt, this distortion would have been much less marked if separation had been done as soon as the unequal growth of the fingers became evident. Division of the webs with closure of the skin edges by suture in another clinic resulted in gangrene necessitating amputation of the distal phalanx of the left little finger. It was necessary subsequently to shorten the phalanx, remove the scar tissue and skin graft the remaining defect before a satisfactory stump was finally obtained. The right hand shows the separation of the fingers nearly completed. The commissure is higher than normal and should be lowered. When this is done, full separation of the fingers will be possible. This case illustrates the importance of preserving the blood supply and the danger of approximating the skin edges under too much tension.

In a case of complete fusion of the third and fourth fingers of the left hand and bilateral incomplete fusion of the second and third toes, there were double great toes on both feet

In a case of complete fusion of the first and second and of the fourth and fifth fingers of the left hand there was a supernumerary little finger on the left hand

In a case of complete fusion of the second and third toes of the right foot, there was right talipes equinovarus

In a case of fusion of the fourth and fifth fingers of the left hand, there was a lymphangioma of the right foot



Fig 14—Bilateral complicated syndactylism of the hands in a girl aged 1 year, who had no family history of syndactylism. The head was quite large. Right hand. The shortened and thickened second finger was united to the end of the fourth finger over the top of the middle finger. The proximal phalanges of the fourth and fifth fingers were fused. Left hand. The third finger was missing except for a portion of the first phalanx, over this the second and fourth fingers were fused. The fourth and fifth fingers were also fused, and the left hand had the appearance of a mitten. The first and second toes of the right foot were missing. It is probable that the fusion of the ends of the second and fourth fingers over the middle finger of each hand was due to the growing together of two raw surfaces which occurred during the process of intra-uterine amputations and that this was not caused by an arrest in normal development. Operative treatment. The fused ends of the second and fourth fingers were divided to allow growth and the raw surfaces were grafted.

In a case of bilateral incomplete fusion of the third and fourth toes, there was bilateral synostosis of the first joint of the fifth finger

In a case of complete fusion of the fourth and fifth fingers of the right hand and incomplete fusion of the second and third toes of the right foot, there were bilateral supernumerary fifth fingers and toes

#### REVIEW OF OPERATIVE PROCEDURES USED IN THE TREATMENT FOR SYNDACTYLISM

In dealing with the treatment for webbed fingers, it is advisable for the surgeon to be familiar with the different types of operations

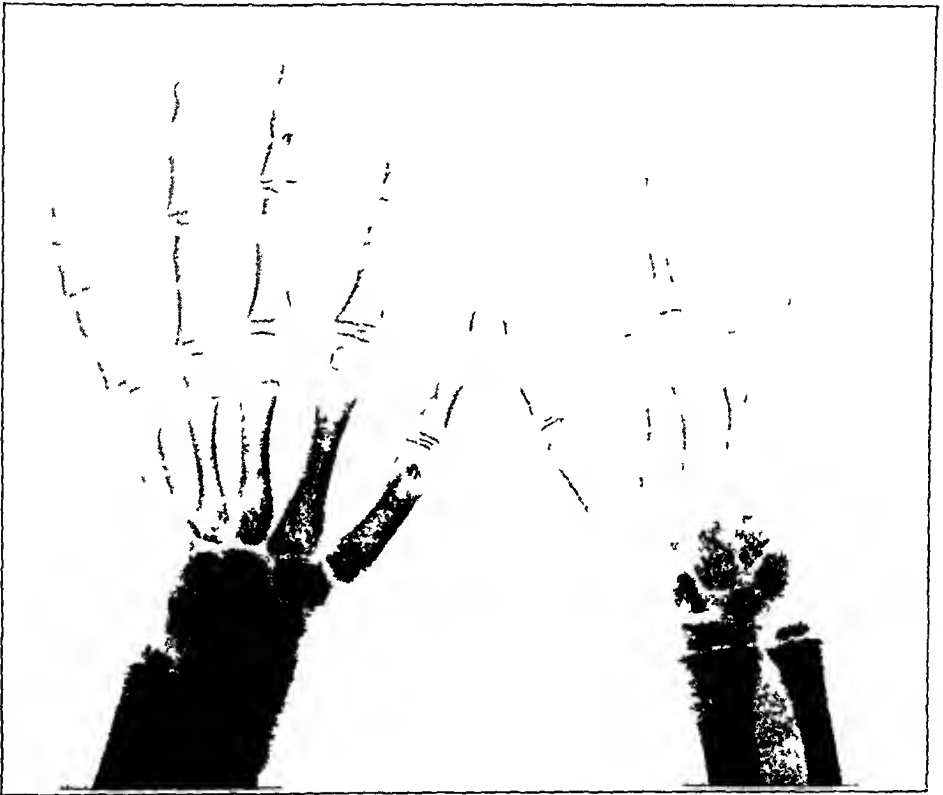


Fig 15—Syndactylism associated with arrested development, in a white child, aged  $5\frac{1}{2}$  years. There was a history of a first cousin of her maternal grandmother having had webbing of the third and fourth fingers. This plate is shown to illustrate the fact which we have noted several times in our series that associated with syndactylism there may be arrested development of the entire hand. There is incomplete fusion of the second, third and fourth fingers. Note the size of all the bones as compared with the normal hand, also the marked shortening of the second phalangeal bones. In this case the fingers were completely separated and the commissures formed, every effort is being made to stimulate the growth of the hand. The function of the individual fingers is perfect.

that have been used at various times as he may be able to utilize points from more than one operative method in dealing with the particular case under consideration.

A review of the literature reveals numerous methods that have been advocated for relief from syndactylism, and we shall outline briefly some of the more important of those which have appeared during the last one hundred and twenty-five years and shall comment on them.

*Rudtorffer's Operation — Volpcau's Operation* — During the earliest times simple division of the web was practiced but this proved unsatisfactory as it was almost always followed by a growth of scar tissue.

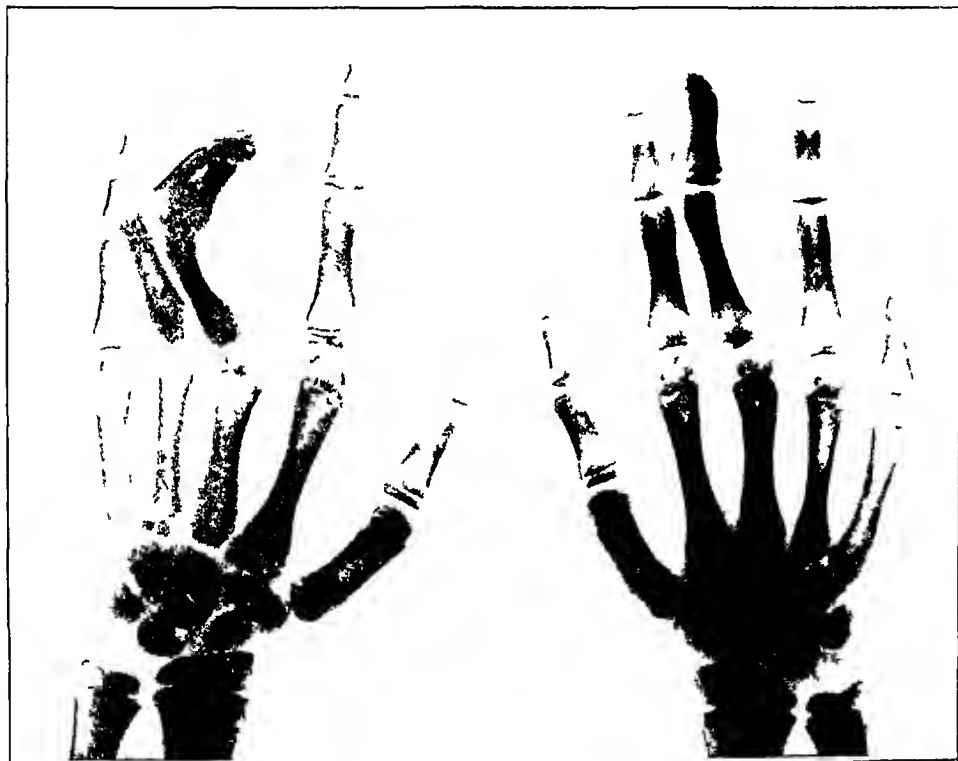


Fig. 16—Roentgenograms of a white boy, aged 11, shown to illustrate a marked case of bilateral syndactylism. Right hand. The second and third fingers are partially fused and although the web does not extend to the terminal phalanx there is marked flexion of the third finger which can be noted in this figure and also in figure 17. Left hand. The third and fourth fingers are completely fused, the nails of the first and second phalanges being also joined. Note the bone distortion and the position of the phalangeal bones. In trying to restore the fingers in a case of this type, the greatest care is necessary and the only method which promised any result is the use of a whole thickness graft to cover the raw surfaces and also form the commissure. In such a case, if there is any doubt about the circulation, it is advisable to separate only the distal portion first and later complete the work.

across the commissure, contraction of the scar and at least a partial return of the original deformity. Rudtorffer,<sup>26</sup> in 1801, modified this

<sup>26</sup> Rudtorffer. Abhandlung ueber die Operation eingekerkelter Brueche nebst einem Anhang, Vienna, J. V. Degau, 1810, vol. 11 p. 478.

procedure by making a tunnel, from the dorsal to the palmar aspect, at the base of the web. A leaden thread was introduced through this opening and was kept in place till the tunnel was lined with epithelium. This cicatrized fistula formed the floor of the new commissure. The web was then divided down into the lumen of the tunnel and the fingers were kept separated until healing was complete. This procedure was moderately successful in the cases with a thin wide web. Later operators



Fig. 17—Same patient as in figure 16. Note the amount of extension possible in the fused fingers.

substituted a silver wire, an india rubber cord or a glass tube for the leaden thread. Velpeau<sup>27</sup> made use of Rudtorff's procedure, but improved on it by suturing the edges of the skin along each finger after division of the web down to the epithelialized tunnel.

This method is far from satisfactory, as the commissure thus formed is usually narrow and is liable to split. In fact the procedure is now seldom used by any one who is familiar with the modern surgical treatment for fused fingers.

<sup>27</sup> Velpeau. *Operative Surgery*. Townsend and Mori. New York: 1883. Wood 1847 vol. 1 p. 386.





Fig 18—*A*, complete bilateral syndactylism of the complicated type in a girl, aged 6, with congenital bilateral fusion of the ring and middle fingers and with bony union of the terminal phalanges of these fingers on the right hand. There was a family history of similar developmental deformities in the maternal great grandfather, both hands, in the maternal grandfather, right hand, and in the mother, right hand. *B*, note the double terminal phalanx of the left ring finger and the abnormal bony growth on the radial side of the second phalanx near the joint. There is also a double terminal phalanx on the right ring finger, which is fused with the terminal phalanx of the middle finger. This is rather an unusual type of bone fusion. It can be noted in *B* that the nails on the right hand, where the bony fusion is closest, have a distinct groove separating them, while on the left hand where the fusion of the bones is lacking, the nails are closely fused. The lateral distortion of the terminal phalanges and the slight angling of the joints are to be noted, this is due to the fusion of fingers of unequal length. Early separation of these terminal phalanges would probably have minimized the lateral tilting. *C*, ten years after operation. Great improvement followed the separation of the fingers but it can be noted that there is still some distortion of the terminal phalanges of both ring fingers. In this case the commissures could be deepened considerably and possibly the terminal phalanges straightened. The function of the hand is excellent and the patient has hesitated to undergo further operative work.

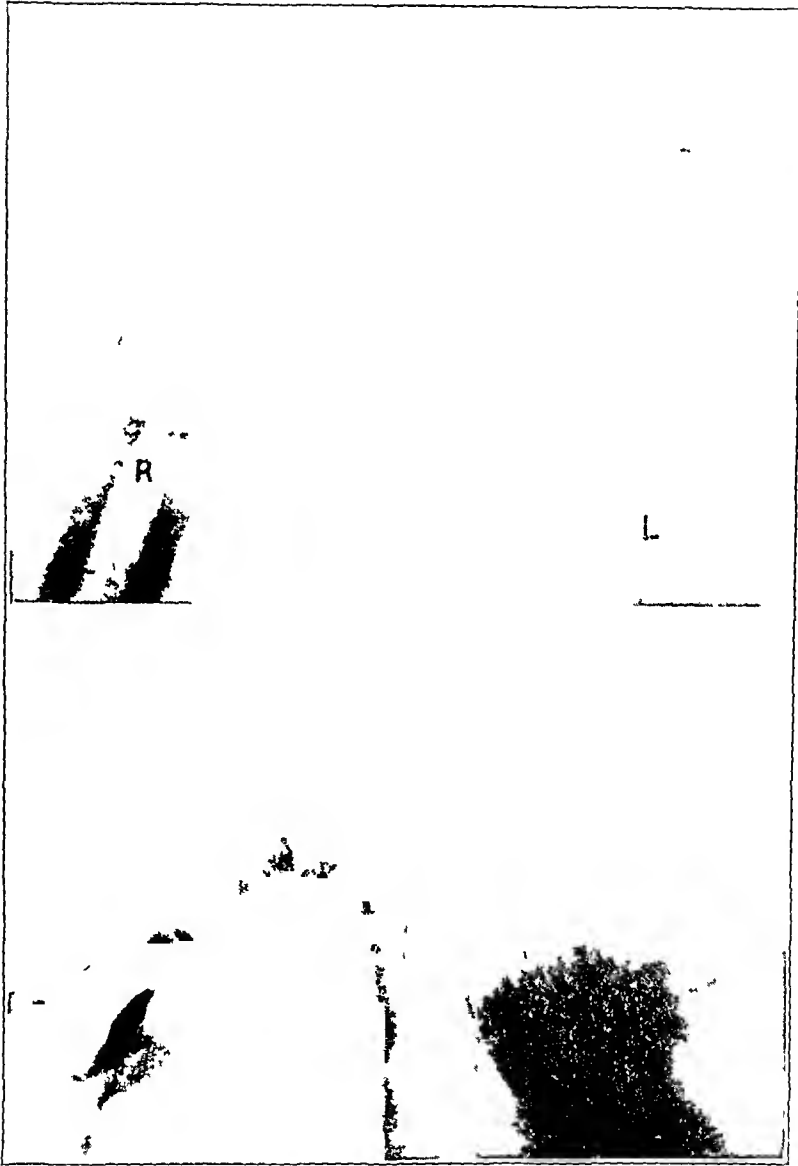


Fig 19—Syndactylism, missing metacarpals and phalanges and crabclaw feet in a white child, aged 18 months with a history of the mother having complete unilateral syndactylism of the second and third toes of the left foot. This case is interesting from the fact that on the right hand the first and second fingers with their metacarpal bones are missing, also the phalangeal bones of the third finger and the two distal phalanges of the fourth finger, although there is apparent fusion of the stumps of the third and fourth fingers. On the left hand, there is complete fusion of the fourth and fifth fingers. The thumb with its phalanges and metacarpal bone is missing, as are the phalanges of the second finger and with the exception of a small fragment, those of the third finger. Both feet are of the typical crabclaw cleft type. In this case, the first step was the preliminary separation of the fourth and fifth fingers of the left hand to allow normal growth

*Zeller's Operation*—In 1810 Zeller<sup>28</sup> introduced the flap method. He raised a short V-shaped flap on the dorsal aspect of the root of the web, the base of the flap corresponding to the position of the normal commissure (fig 20). After division of the rest of the web, the apex of the flap was drawn through between the fingers and sutured to the palmar aspect, thus forming and lining the commissure. The tendency for sloughing to occur at the tip of the V-shaped flap led



Fig 20—Same patient as in figure 19

Dieffenbach<sup>29</sup> to adopt a flap of quadrilateral outline which was utilized in the same way. Another modification of this operation was described by Norton,<sup>30</sup> who made use of two triangular flaps, one from

28 Zeller. Ueber der ersten Erscheinungen venerischen Localkrankheit, Vienna, J. G. Binz, 1810, p. 109.

29 Dieffenbach, F. J. Chirurgische Erfahrungen besonders über die Wiederherstellung zerstörter Teile des menschlichen Körpers nach neuen Methoden, Berlin, T. C. F. Enslin, 1834.

30 Norton, A. T. A New and Reliable Operation for the Cure of Webbed-Fingers, Brit. M. J. 2 931, 1881.

the dorsal and the other from the palmar aspect, which were carried between the fingers from opposite directions to form a new commissure. The principle of Zeller's operation was also used in the method of Deces and that of Morel-Lavalle.<sup>31</sup> The use of a flap, either single or double, for forming the commissure was a distinct advance in the treatment for this deformity, and we frequently use it in one form or another with considerable satisfaction.

*Didot's Operation*—This method has been attributed to Didot,<sup>32</sup> Diday<sup>33</sup> and Nelaton.<sup>34</sup> Didot described the method in 1850, while an



Fig. 21—Syndactylism, associated with double great toes, in a negro boy, with no family history of similar trouble. There is almost complete fusion of the third and fourth fingers of the left hand, also bilateral incomplete fusion of the second and third toes and bilateral double great toes. Note that the terminal phalanges of the webbed fingers are not completely adherent and that the separation present has prevented the marked distortion which ordinarily would have occurred had the fusion been complete between these fingers. It can be seen, however, that there is considerable pull exerted by the third finger, and further separation was advisable in order to avoid lateral curving of the digits before the formation of the commissure and the final complete separation of the fingers. As far as the feet are concerned, the webbed toes should not be disturbed. Except for the width of the feet there is no need for interference with the double great toes in this particular case.

abstract of Diday's paper appeared in the same year (fig. 21). Nelaton's article on the subject was not published until 1884. The principle

31 Morel-Lavalle. Cas de syndactylie chez un homme, *Compt. rend. Soc. de biol.* **1** 166, 1849-1850.

32 Didot, A. *Acad. roy. de Belg.* **9** 351, 1849-1850.

33 Diday, A. *J. f. Kinderkrankht.* **15** 470, 1850.

34 Nelaton, A. *Elements de pathologie chirurgicale*, Paris, Germer-Bailliere et Cie, 1884, vol. 6, p. 1020.

consists of the production of two short, broad-based quadrilateral flaps, the first with its pedicle on the dorsum of one of the united fingers and the second with its pedicle on the palmar aspect of the other finger. The breadth of the flaps corresponds to the length of the web, and then length should correspond to the width of the raw surface each flap has to cover. After the flaps have been raised the remaining tissue uniting the fingers is divided in the midline, interference with the circulation being avoided if possible. The flaps are then swung around to cover the raw surface of the finger to which each is attached, and are sutured in place. On paper this is an attractive procedure but in actual practice we rarely use the method, especially when the fingers are closely fused, as the flaps are seldom sufficiently long to cover the defect. Consequently, when the closure is made, care must be taken to avoid too much tension on the flaps, as this in some instances may obstruct the circulation sufficiently to cause gangrene of the finger. In this type of operation the fingers are separated and theoretically covered, but no provision is made for the formation of a true commissure. This may be formed, however, by a skin graft or a flap from a distant part.

In certain instances when there is sufficient skin to assure flaps by Didot's method which are long enough to be sutured without tension, the preliminary formation of a skin-lined tube at the base of the web to form the commissure might be considered.

*Agnew's*<sup>35</sup> *Operation* (1883) —This procedure is used when the web is quite wide, and it is really a modification of Zeller's operation but differs from the latter in having the V-shaped flap extend to the distal margin of the web. The flap is raised from the dorsum of the web, with its base at the metacarpophalangeal joint. After division of the remaining portion of the web, the flap is sutured to the palm, and the lax skin of the palmar surface is used to close the raw surfaces of the fingers (fig 22). In using this procedure we have found that a blunt pointed flap is more practical than one with a sharp point.

*Félizet's*<sup>36</sup> *Operation* (1892) —This operation is almost identical with the modification of Zeller's operation practiced by Norton. Two small triangular flaps are raised at the base of the web with their apices pointing distally. One flap is on the palmar and the other on the dorsal aspect of the hand (fig 23). After the web is divided, the flaps are drawn between the fingers and are sutured side by side to form the new commissure. This procedure insures the formation of a broad,

35 Agnew, D. H. *Principles and Practice of Surgery*. Philadelphia, J. B. Lippincott Company, 1889, vol. 3, p. 371.

36 Félizet, G. *Rev. d'orthop.* 3:49, 1892.

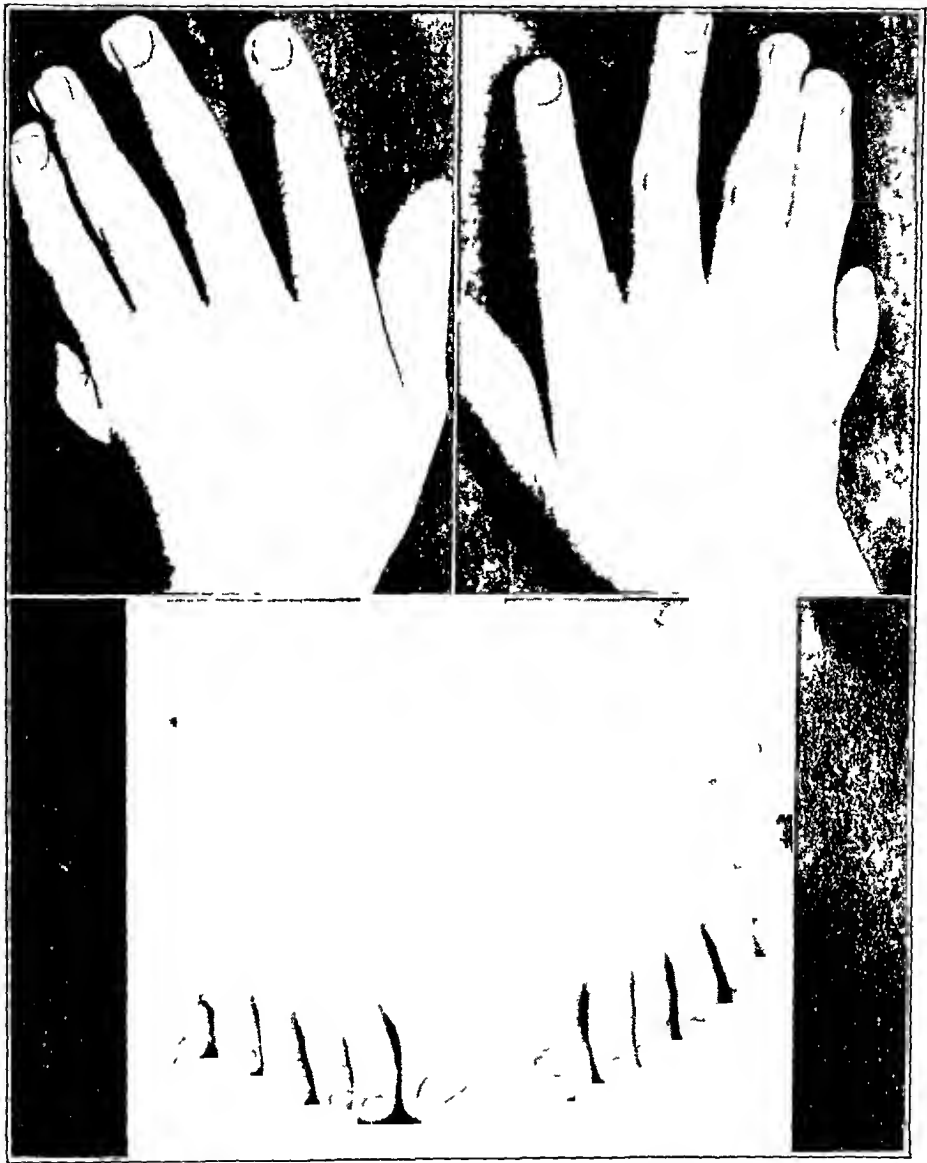


Fig 22—Incomplete simple unilateral syndactylism of the right hand and toot, associated with bilateral polydactylism of the hands and feet, in a boy, aged 6 years, who had a family history of syndactylism in the father, a sister, a granduncle and a cousin on the paternal side. There is fusion of the fourth and fifth fingers of the right hand which extended nearly to the nails. There is incomplete fusion of the second and third toes of the right foot. There are also bilateral supernumerary fifth fingers and toes. Roentgen examination showed the bones to be normal. The web was divided, and the skin which was slack was sutured, thus covering both fingers. The commissure was made by utilizing the skin of the supernumerary fingers. A perfect functional result was obtained. The age of this patient was about right to begin operative work.

thick commissure, and with modifications made to suit conditions it is useful. The raw surfaces may be closed by sutures if the skin is lax, otherwise they must be grafted.

*Bidwell's Operation (1913)*—This operation is practically a combination of Zeller's and Didot's operations and consists of the production of a V-shaped flap on the dorsum at the base of the web and a lateral flap of the Didot type on the dorsum of one of the fused fingers. A straight incision is made through the palmar portion of the web to insure normal skin on the palmar surface of the fingers. The dorsal V-shaped flap is sutured to the palm, after division of the web to make the commissure and the lateral flap is sutured to the edge of

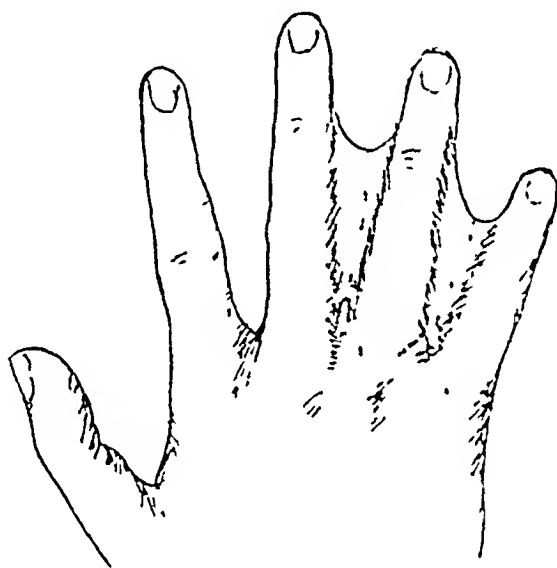


Fig. 23—Zeller's operation for syndactylism. Zeller, in 1810, was the first to suggest the use of a flap to form the commissure. In this drawing the webs were lax and thin. The dotted lines indicate the incisions. Note the short pointed flap outlined at the proximal end of the web. The fingers were separated, the flap was raised and drawn between the fingers. The tip was then sutured to the incision on the palmar surface, thus forming the commissure.

the skin of the palmar aspect of the finger to which it is attached (fig. 24). This leaves an extensive raw area on the dorsum and inner aspect of one finger, which should be covered by a skin graft. The procedure may even be used in cases in which the web is very narrow, and should be borne in mind, as the commissure is formed with a flap and one finger is covered with skin, leaving only a single area to graft. The choice of fingers to cover with the flap is important.

37 Bidwell, L. A. *Minor Surgery*, ed. 2, New York, William Wood & Company, 1913, p. 90.

*Famel's Operation (1911)*—This is a modification of Didot's operation in which a Z-shaped incision is made on the dorsal and palmar surfaces of the web, in place of the usual quadrilateral flaps (fig 25). Each Z is resolved into two V-shaped flaps on the front and back of the web, and these are brought around and sutured to form the inner surface of each finger. The tips of the V-shaped flaps are likely to slough if there is any undue tension.

*Tubby's Operation (1912)*—Tubby<sup>39</sup> made use of the principles of Rudtorffer, Zeller and Didot, and his operation is practically identical with one of the methods previously described by Felizet. Two flaps are cut at the base of the web, the palmar with its base toward the tips of the fingers and the dorsal in the opposite direction (fig 26). The soft parts between the flaps are removed, and each flap is drawn through this opening and sutured so as to line it as completely as possible. A

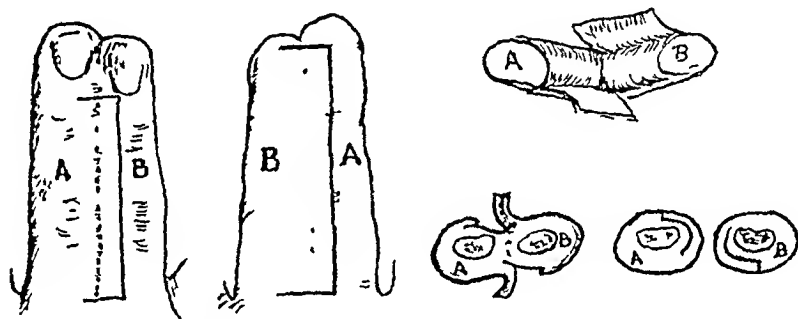


Fig 24—Didot's operation for syndactylism. The drawing shows the fusion of two fingers, A and B. The solid line indicates the incision made in raising the palmar flap with its base on B. A similar flap is raised on the dorsal surface of the fingers with its base on A. The dotted line shows the site of the midline separation of the fingers after the flaps are raised. After the fingers have been separated, the flap with its base on B is brought around and sutured to fill the defect on B, which is left by raising the flap with its base on A. The flap on A is used in a similar manner to fill the defect on this finger. The transverse sections indicate the manner in which this procedure is carried out.

glass rod is then passed through the opening and is held in place by supports projecting from a metal cuff fastened about the wrist. When the foramen has completely healed, the second stage is carried out as in Didot's operation, and the glass rod is again placed in position to insure the maintenance of the commissure in its normal location. This seems the rational place to use Didot's operation, if there is sufficient

38. Famel, H. Syndactylie, modification du procede de Didot. Scalpel, Liege 64 254, 1911.

39. Tubby, A. H. An Operation for Webbed Fingers. Brit. M. J. 2 1464 (Nov. 23) 1912.



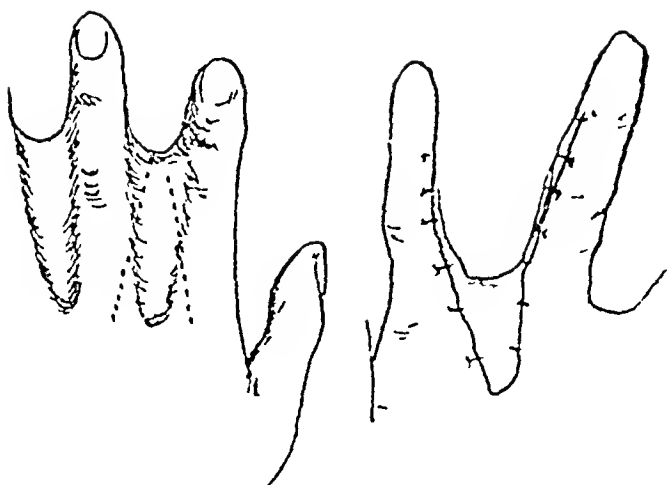


Fig 25—Agnew's operation for syndactylism. The drawing shows a lax web. The dotted line indicates the incision made to form the flap. Note that the flap is long and extends to the margin of the web. The drawing shows the flap much more blunt than that originally used by Agnew. The flap is raised and after a midline separation of the fingers, it is brought forward between the fingers to form the commissure and is sutured in position. The skin on the fingers is closed by sutures.

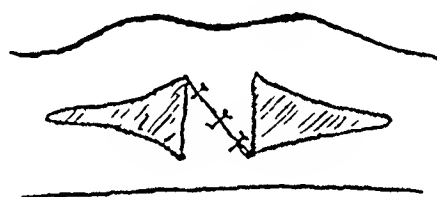


Fig 26—Fehizet's operation for syndactylism (Davis, J. S. Plastic Surgery, Philadelphia, P. Blakiston's Son & Company, 1919, p. 239). Two small triangular flaps, one from the palmar and the other from the dorsal surface, are raised from the base of the web with their apices pointing distally. The fingers are separated and the flaps are brought down and placed side by side and sutured, thus forming the commissure. If the skin on the fingers is lax the edges may be sutured, otherwise the defects left must be covered with whole thickness grafts.

skin to close without tension, as the commissure is formed before the fingers are released, however, we have seldom found it necessary to form a commissure by means of a permanent fistula

*Radulesco's*<sup>40</sup> *Operation* (1923) —This operation is somewhat similar to Faniel's operation. The dorsal and palmar incisions are made in the form of an inverted question mark instead of a Z, the dorsal flap extending as low as the metacarpophalangeal joint, and the palmar flap not quite so low. This eliminates the sharp apexes that have a tendency to slough, and is an improvement over Faniel's procedure. The flaps are sutured in place to form the inner aspects of the fingers and also the commissure (fig 27). The method is well worth bearing in mind and will be found useful. This operation, as well as that of

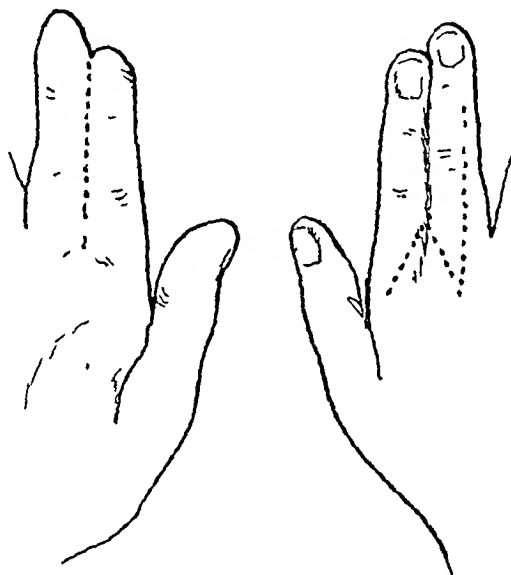


Fig 27 —Bidwell's operation for syndactylism. The dotted lines indicate the incisions. The triangular flap at the base of the web is drawn forward after the fingers are separated and forms the commissure. Note the wide flap to be raised from the back of the middle finger which has its base on the dorsum of the index finger and which will be brought around to cover the defect on the index finger. This, of course, leaves a large uncovered surface on the middle finger which should be covered with a whole thickness skin graft.

Faniel, depends on the shifting of flaps cut in different ways, and the vitality of these flaps depends largely on whether or not they can be sutured without tension.

*Villechaise's*<sup>41</sup> *Operation* (1927) —This is a modification of the procedures of Didot and Agnew, applicable in cases in which there is a

40 Radulesco, A. D. Un nouveau procede operatoire digito-commisural comme traitement de la syndactylie congenitale, *Rev d'orthop* 30 499, 1923, *Abstr, Internat Survey Surg*, February, 1924, p 257.

41 Villechaise, and Jean, G. Quelques points de technique concernant la chirurgie de la syndactylie, *Rev d'orthop* 14 241, 1927.

wide web between the fingers. In place of the dorsal V-shaped flap of Agnew, a palmar quadrilateral flap is raised, with its base at the metacarpophalangeal joint (fig 28). When drawn between the separated fingers, this flap forms the commissure. In place of the dorsal and palmar finger flaps of Didot two dorsal finger flaps are made to form the inner surface of the fingers. In cases in which there is a narrow web, a long pedunculated flap is raised, with its base at the metacarpophalangeal joint and its apex extending proximally along the dorsum of the hand. The web is then divided and the flap is swung around to cover the inner surface of one of the fingers. This procedure is also advocated by Forgue<sup>42</sup> (fig 29). The difficulty is that no pedunculated flap as long as that shown in the illustration and with as narrow a pedicle can live in such a situation unless it is carefully

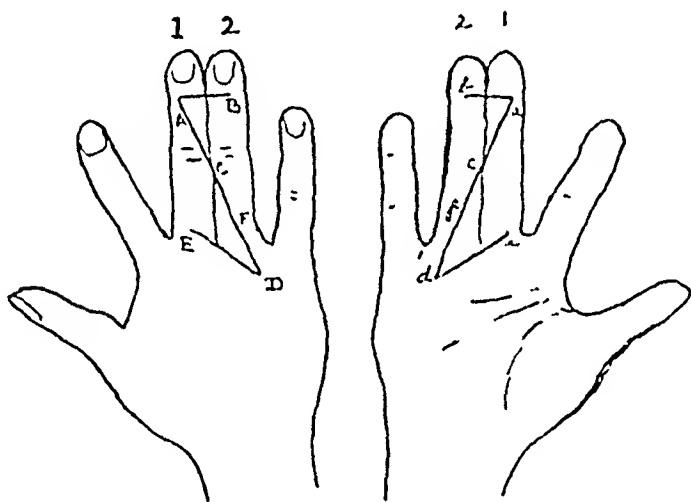


Fig 28—Faniel's operation for syndactylism. The drawing shows fusion of the third and fourth fingers designated 1 and 2. A transverse incision  $A-B$  is made at the most distal point of the fusion. This includes half of the skin of both fingers. From  $A$ , an oblique incision,  $C-D$ , is made to the center of the base of finger 2, ending near the metacarpophalangeal joint. From  $D$  an incision is carried to the middle of the base of the proximal phalanx which ends a little higher than the level of the future commissure, a line from  $E$  to  $F$  being parallel to  $AB$ . This forms the flaps  $BAC$  with its pedicle on finger 2, and  $CDE$  with its pedicle on finger 1. The same incisions, reversed, are made on the palmar surface of the fingers and two other flaps thus formed. The four flaps are dissected up, the fingers are separated and the flaps are sutured into the positions into which they fall.

prepared as a delayed transfer of the double pedicled variety, with subsequent division of the outer pedicle. However, it might live as would a graft if it consisted of the skin alone, but in our opinion a

<sup>42</sup> Forgue, L. D. Syndactylie membraneuse congenitale du medius et de l'annulaire des deux mains operation. *Arch de med et pharm mil* **27** 128 1896

whole thickness graft would be preferable, as it could be obtained without damage to the hand

*Stone's Operation (1908)*—J S Stone<sup>43</sup> devised a method for covering the index and little fingers with skin in cases in which there is fusion of the second, third, fourth and fifth fingers. A dorsal longitudinal incision is made along the full length of the web between the ring and middle fingers, and transverse incisions are made on each side of this incision at the base and apex of the web thus forming two dorsal quadrilateral flaps. The pedicles of these flaps are on the index and little fingers. The webs attached to the index and the little fingers are then divided and the flaps on the dorsa of these fingers are swung around and sutured to the palmar aspect, thus covering these fingers with skin (fig 30). The middle and ring fingers are still fused but are denuded of skin on their dorsal surfaces. This raw surface may

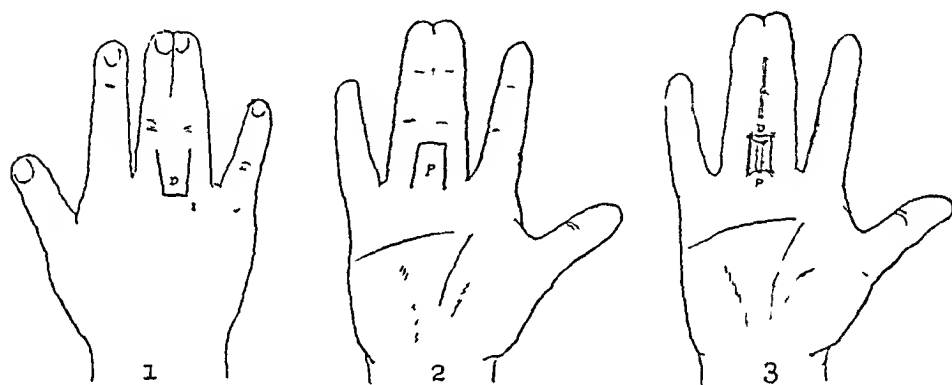


Fig 29—Procedure of Felizet (Berger and Banzet. Treatment of Syndactylism, *Chir Orthop*, 1904, p 278). 1 shows the incisions made outlining the dorsal flap *D* with its pedicle toward the tips of the fingers. 2 shows the incisions outlining the palmar flap with its pedicle toward the palm. 3 shows the buttonhole made between the fingers after the flaps are raised with the dorsal flap lining the distal end and the palmar flap the proximal end. The sides of the buttonhole are allowed to heal by granulation. By this procedure the commissure is formed. Note the elastic ligature above which is passed through the web and is tightly tied, which is eventually supposed to complete the separation but today is seldom, if ever, used. The formation of the commissure by this method is practically the same as that subsequently described by Tubbi, but instead of using the elastic ligature, he utilizes Didot's method for covering the fingers.

be covered by a graft, a gauntlet flap or a pedunculated flap from the abdominal wall. This operation provides for the separation of two of the fingers and then being covered with skin flaps but this is only the first step as wide commissures have to be formed before the fingers can function properly. The ring and middle fingers can subsequently be

<sup>43</sup> Stone J S. *American Practice of Surgery*. New York: Wm Wood & Company, 1908. vol 4. p 634.

separated and at the same time a commissure formed either by the use of a flap of the intact skin with grafting of skin when necessary, or by simple division of the web followed by lining the raw surfaces and forming the commissure with single whole thickness graft by the method described later. Stone's operation is based on Didot's quadri-lateral flap method but he secures both flaps from the back of the middle and ring fingers rather than one from the dorsal and one from the palmar surface. This leaves a single broad denuded area which is much easier to cover with a skin graft or flap than the narrower denudations that result when the flaps are raised from the front and back of the fingers to be covered. The utilization of the skin from the entire dorsal surface of the fused middle and ring fingers gives a flap of sufficient size to cover the fore and little fingers without tension.

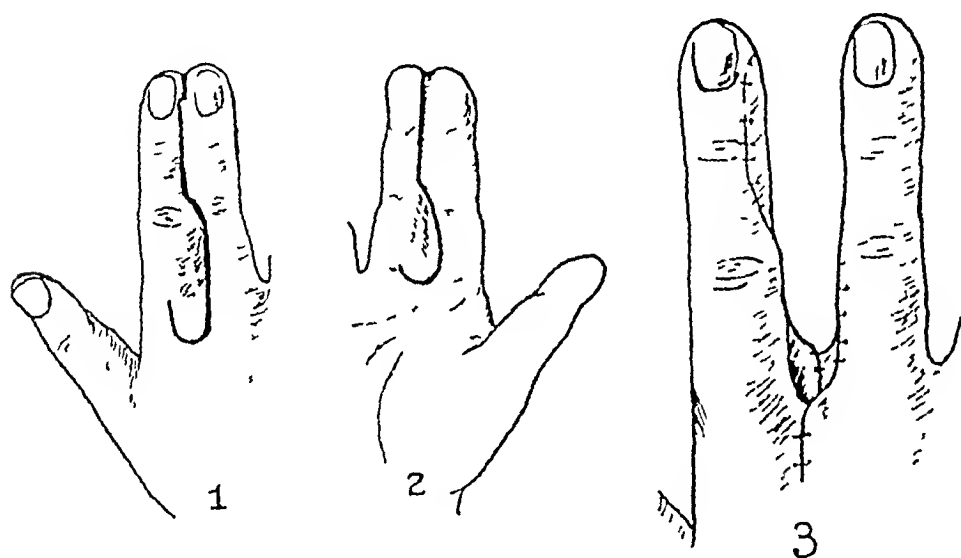


Fig. 30—Radulesco's operation for syndactylism. 1 and 2, the dark lines indicate the incisions made in raising flaps which will cover in the fingers and also form the commissure. 3 shows the flaps sutured in place.

#### METHODS FOUND USEFUL BY AUTHORS IN THE TREATMENT FOR CONGENITAL SYNDACTYLISM

A glance at the summary of our series of cases and at the illustrations will give an idea of some of the varieties of the deformity, and will indicate clearly that the problem of reconstruction is far from simple. As a matter of fact, in certain instances complete restoration of normal function may be impossible.

Experience has shown us that no single operation has yet been developed which can be used in relieving all types of syndactylism. Each case must be studied carefully, and the method or combination of methods selected which will be most effective for the individual case. The cure of syndactylism, even in the simpler cases, is not as easy as

some of the drawings and operative descriptions would lead one to believe. In fact, a good result is a difficult matter to accomplish, and it is frequently necessary to operate several times before the desired outcome is obtained.

*Most Suitable Age for Operation*—In the instances in which there is complete fusion of fingers of unequal length with coherence of the terminal phalanges on the same level, development is interfered with and marked secondary deformity will be produced unless the fingers are separated sufficiently to allow the independent unhindered growth of both fingers. This separation should be made as early as the inequality of growth becomes apparent, however young the child may be. We usually separate the fingers in the midline and cover the raw surfaces with a whole thickness skin graft. This procedure, which is all that should be done at this period, usually gives the fingers an opportunity to grow, and often prevents lateral bending of the phalanges.

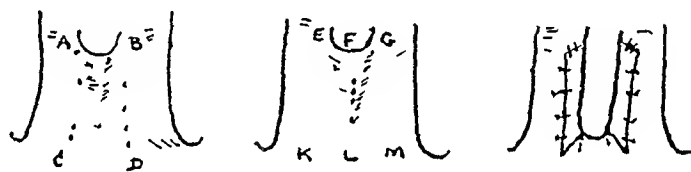


Fig. 31—Villechaise's operation for syndactylism. A palmar flap, *CABD*, is formed, then two dorsal flaps, *EFLK* and *GFLM*. The fingers are separated, and the flap *CABD* is carried backward between the fingers and sutured to form the commissure. Then the two dorsal flaps are brought forward and sutured to fill the defects on the fingers.

On the other hand, we feel that in the majority of cases, it is poor surgical judgment to operate for complete relief from this malformation and to attempt the formation of a wide commissure before the child is 6 or 7 years old. We say this advisedly as in the instances in which early complete operations have been done, here and elsewhere, it is almost always necessary to do them over again when the child grows older. We often see patients whose hands have been operated on several times for complete relief from syndactylism before they are 6 months old, and some of them are in such condition that it takes years of work and numerous operations to salvage the fingers so that they may become even partially useful. In several instances in which function could not be restored, we have had to amputate the deformed fingers.

*Operative Treatment*—The key to the success of any operative procedure undertaken for relief from syndactylism is the formation of a satisfactory commissure between the fused fingers, and in order to

allow for subsequent shrinkage this commissure should be made somewhat deeper and wider than that between the normal fingers. When one is dealing with a web that does not hold the fingers closely together, or in other words with a lax web, several procedures may be tried. A useful method is to raise a long dorsal flap, which is much more blunt than that suggested by Agnew, and which has its pedicle toward the wrist on the level of the metacarpophalangeal joints. After a midline division of the palmar surface of the web down to the same level, a short transverse incision is made on each side, forming an inverted T. The flap is drawn forward between the fingers to form the commissure and is sutured to the transverse portion of the T. The skin on the fingers is then sutured. We use horseshoe sutures exclusively in all of these cases. We find, however, depending on conditions, that shorter dorsal

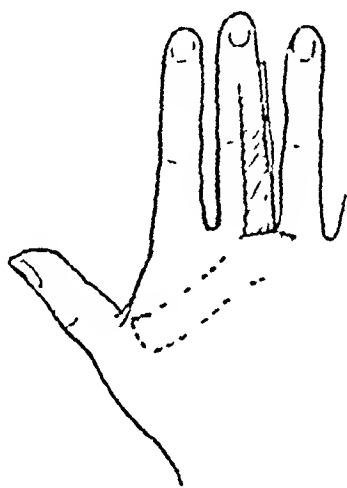


Fig. 32—Forgue's operation for syndactyly (Villechaise and Jean). The dotted line shows the incision made in raising a pedunculated flap from the dorsum of the hand, to be used in covering the raw surface of one finger after division of the web. The circulation of this flap would be more assured if one of the methods of delayed transfer were used rather than an immediate transfer.

and palmar flaps which may be either sutured end to end or side to side are often preferable for forming the commissure. If the skin of the fingers is lax and can be closed without tension, we suture it over the raw surfaces, but when there is tension, it is preferable to cover the raw surfaces with whole thickness skin grafts.

When the web is comparatively short and wide and does not extend further than the proximal phalangeal joint, we find the use of the Z incision with transposition of the flaps thus formed most helpful. In these cases, we make an incision along the rim of the web between the fingers and separate the web into two leaves. The arms of the Z are formed by incisions beginning at the ends of the primary incision, that on the dorsum extends from one end of the primary incision diagonally

across until it reaches approximately the level of the metacarpophalangeal joint between the bones, that from the other end extends diagonally on the palmar surface to a point opposite the lowest end of the dorsal incision. When the arms meet the primary incision, it is advisable to curve the incision so that the end of the flaps will be blunt rather than pointed. By undercutting the tissues outlined by these incisions two flaps are formed. These are raised and transposed, the tip of each flap being sutured into the extremity of the incision making the opposite arm of the Z, and the adjacent margins are sutured, thus releasing the web and forming a good working commissure.

When the fingers are closely fused, we proceed in either one of two ways, depending on conditions. In one group of cases, we form the commissure by means of two pedunculated flaps, one of which is raised on the dorsum of the fused fingers, with its base toward the wrist

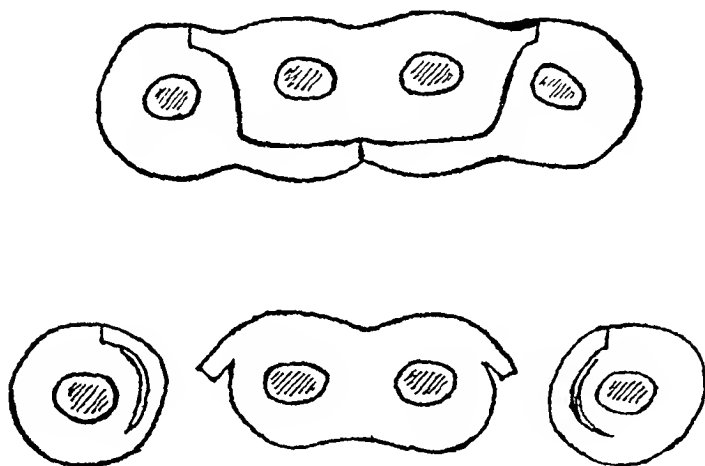


Fig. 33—Stone's operation for syndactylism. This operation is devised to cover the index and little fingers in the cases in which there is fusion of all the fingers. A dorsal longitudinal incision is made along the full length of the web between the ring and middle fingers and transverse incisions are made on each side of this incision at the base and apex of the web, thus forming two quadrilateral flaps, the bases of which are on the index and little fingers. The index finger is separated from the middle finger, and the little finger is separated from the ring finger. The flaps are then brought around and will cover the defects completely. The raw surface on the dorsum of the middle and ring fingers is covered with a whole thickness graft or a pedunculated flap from a distant part.

about on the level of the metacarpophalangeal joint and the other on the palm on about the same level. Each flap should be sufficiently long to be able to pass between the separated fingers and be sutured without tension, the dorsal flap to the end of the palmar incision and the palmar flap to the end of the dorsal incision. The flaps should be blunt and as thick as possible in order to assure their blood supply. When the flaps touch as they lie adjacent to each other, the edges



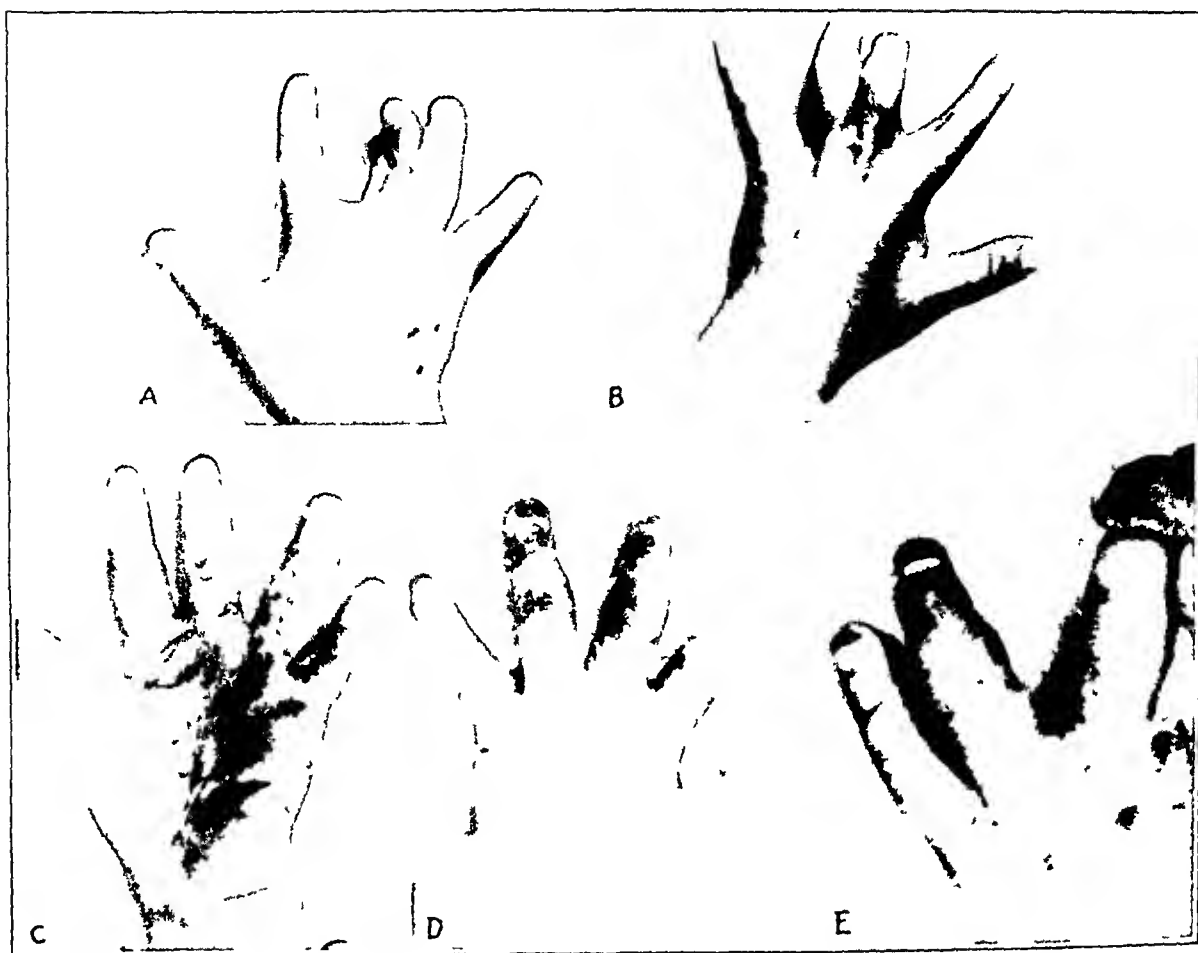


Fig 34—A white boy, aged 6 years, with no family history of syndactyism, showing the result of three previous operations performed elsewhere to relieve the defect. The first operation was done when the patient was 4 months old, and the others within the first eighteen months. This picture is not an uncommon one and illustrates our reason for not doing the complete operation at an early age. *A* and *B* note the recurrent web extending beyond the proximal phalangeal joints, also the flexion of the fingers due to scar contracture. Scars outlining the flaps which were originally used to form the commissure can be seen at the base of the fingers. *C* and *D*, result three weeks after the secondary operation. The commissure was formed by blunt pointed anterior and posterior flaps which were drawn between the separated fingers and laid side by side. The tip of the palmar flap was sutured to the defect on the dorsum of the hand and the dorsal flap to that on the palmar surface. Where the edges of the flaps came in contact, they were sutured. The contracture of the fingers was then relieved as completely as possible by excision of scar and stretching. Then into the raw surface on each finger was sutured a measured whole thickness graft. A seasponge dressing was applied which was not disturbed for eighteen days. Note the depth and width of the commissure, also the grafts which have healed nicely. There is still slight flexion of both fingers, but it is probable that active use and massage will overcome this. *E* Five weeks after operation.

are sutured. By this method a good commissure can be obtained, but at the sacrifice of a certain amount of the skin of both fingers, which in the closely fused cases, absolutely prevents closure of the edges of the skin by sutures and leaves a raw surface of varying size on the inner surfaces of both fingers. In order to cover these raw surfaces we use measured grafts of thin hairless whole thickness skin, usually obtained from the inner side of the arm, upper inner part of the thigh or prepuce, and sew these grafts into place with horsehair.

In another group of cases with very close fusion extending to the end of the fingers, we simply separate the fingers carefully along the normal line of division exactly in the midline and carry the separation back nearly to the level of the metacarpophangeal joints. This procedure leaves a raw surface on the inner side of both fingers extending to the bottom of the proposed commissure. The fingers are separated quite widely and the outline of the defect is made with a piece of perforated cellosilk. This outline is transferred to the area from which the graft is to be taken, and a single whole thickness graft is cut and transferred to cover the raw surface and is sutured into place with horsehair. In this way a single measured whole thickness graft fills the defects on the sides of both fingers and also forms the commissure, in many instances, we consider this procedure the method of choice.

*Method of Dressing*—We have found the following to be the most satisfactory dressing after the separation of the fingers and use it as a routine measure whether flaps or grafts, or both, have been employed in the reconstruction. The fingers fully extended are widely separated, and after a few layers of silver foil are applied, one thickness of gauze impregnated with 3 per cent xeroform ointment is placed evenly over the grafts or flaps. A strip of sterile moist seasponge is drawn down snugly over the newly formed commissure. Then the space above it between the fingers is packed quite tightly with pieces of seasponge until it is completely filled. Narrow pieces of sponge are inserted between adjacent fingers, and a large flat strip is placed on the front and another on the back of the hand, thus covering the fingers on all sides with the sponge. The whole is secured under even pressure by a bandage to fix the sponges and immobilize the fingers. An anterior hand and forearm splint is then applied. The tips of the fingers should be visible to check on the circulation. This dressing is left undisturbed for from two to three weeks, and when it is removed, the commissure is formed and the healing of grafts and suture lines is complete. Subsequently the sponge pressure may be reapplied if considered necessary, but ordinarily simple gauze will be sufficient until protecting dressings are unnecessary.

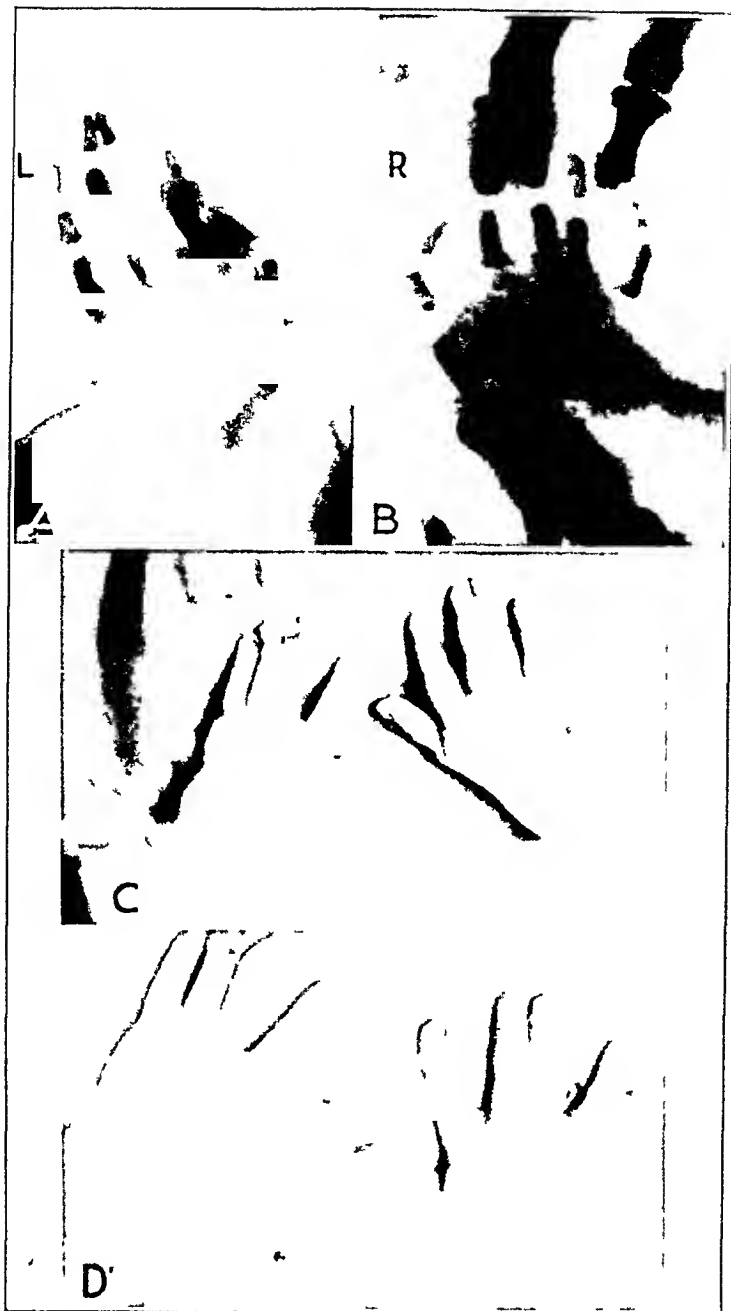


Fig 35—A white boy, with a family history of syndactylism. The father, father's sister and paternal grandfather all had webbed toes, no webbing of the fingers was previously noted. There had been two other children born since this one who have had no sign of syndactylism. *A* and *B*—x-ray plates taken when the patient was 1 day old. Note the shadow of the supernumerary finger on the proximal phalanx of the little finger of the right hand. There was also a smaller supernumerary finger attached to the terminal phalanx of the little finger of the left hand. Right hand. The third and fourth fingers were completely adherent to the tip but there was no fusion of the bone or nail. Left hand. There was fusion of the third, fourth and fifth fingers. There was fusion of the bone of the terminal phalanges of the third and fourth fingers, and the nails were also fused. The large phalangeal bones seen in the pictures are those of the nurse who held the hands. Toes. There was bilateral webbing of the second and third toes, nearly complete on the left foot. When the patient was 11 months old, the terminal phalanges of the third and fourth fingers of the left hand were separated. *C*, result of first operation. *D*, result of subsequent operations to prevent deformity and to allow normal growth. Note the separation of the fingers and that there has been no attempt to form wide commissures, also that the fingers have grown straight except the terminal phalanges of the third and fourth fingers of the left hand. In this case, there had been fusion of the bone and no lateral ligaments were present in the fused side, which would account for the tilting of the terminal phalanges.

## TREATMENT FOR ACQUIRED SYNDACTYLISM

In the operative work for relief from congenital syndactylism, one usually deals with normal tissues. On the other hand, in acquired syndactylism, the tissues dealt with are either entirely scar or are scar infiltrated. Operative procedures that can be successfully carried out in the treatment for the congenital cases cannot be done in the acquired cases, because the blood supply of the scar tissue is insufficient to nourish the necessary flaps. For this reason, the methods of treatment are somewhat limited. In a case of incomplete acquired syndactylism,



Fig 36—Types of acquired syndactylism. *A*, result of a burn. The fingers could not be flexed and there was little separation possible on account of the scar tissue. There is partial fusion between the second and third fingers and between the fourth and fifth fingers, but it is most marked between the third and fourth fingers where the commissure is obliterated and fusion is nearly complete up to the proximal phalangeal joint. Relief was obtained in this case by excision of the scar, followed by the use of a whole thickness skin graft which formed the commissure and covered all raw surfaces. A good functional result was obtained. *B*, result of a burn. The entire hand is covered with scar tissue. The fingers cannot be flexed or spread apart. Note the partial fusion of all the fingers and the obliteration of the web between the thumb and forefinger. Considerable improvement in function was obtained by shifting scar flaps and by the use of whole thickness grafts.

in which the web is fairly wide, it may be possible to relieve the condition by the use of the Z incision as described. The flaps should not be cut as long as when one is dealing with normal tissue but they should be made as thick as possible in order to insure a better blood supply.

When the aforementioned procedure is impracticable on account of the type of fusion, the fingers should be carefully separated and the scar dissected out if possible down to normal tissue. Then into the defect thus formed a single measured whole thickness skin graft should be sutured with horseshan so that it covers the denuded surfaces of the fingers and forms the commissure.

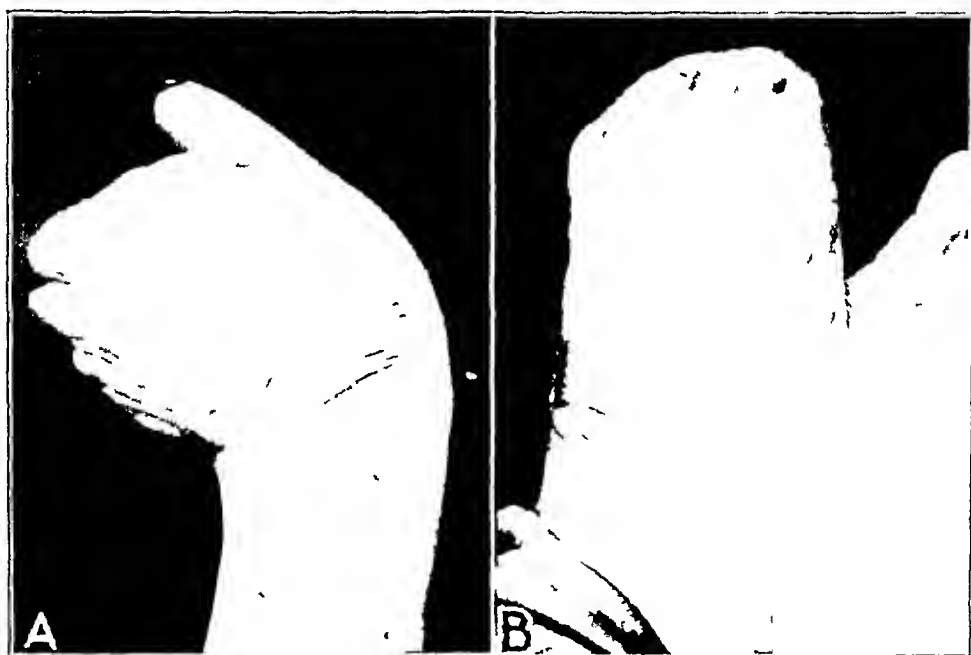


Fig. 37—Types of acquired syndactylism. *A*, result of severe burns. There is lateral scar contracture at the wrist which throws the hand out of line. The stumps of the proximal phalanges of all the fingers are covered with scar tissue and are closely fused. The web between the thumb and first finger is much shortened. In this case the first step was the relaxation of the contracture at the wrist after which the stumps of the fingers were separated and grafted, and the web between the thumb and forefinger was relaxed by a Z incision with the transfer of flaps. *B*, result of a severe burn. The proximal phalangeal stumps are covered by a thin painful scar and are completely fused. The length of the remaining phalangeal bones can be judged by comparing them with the length of the thumb. The stumps moved as one piece. The dimples in the scar are the openings of epithelial lined fistulas which run between the phalanges and are the remains of the original commissures. These have been drawn by scar contracture toward the end of the stump and are much displaced. The process of repair in this case was to remove the thin painful scar and replace it with a pedunculated flap from the abdominal wall which was arranged so that it covered the phalanges on both front and back. Later the finger stumps were separated and the commissures formed so that individual digital motion was possible, and in the end a fairly useful hand was developed.

In some instances in which the fingers are fused and in which there is little hope of securing a worth while functional result on account of the replacement of the integument by dense scar, it is advisable to dissect out the scar and cover the defect with a pedunculated flap. Depending on conditions, a gauntlet double pedicled flap, a tubed flap or some other delayed transfer type of flap may be used. After the flap has grown in place, the pedicle is divided and set in. Then in due time after shrinkage has taken place and the skin and subcutaneous tissues are completely adjusted to their new environment, the fingers may be separated, and the raw surfaces taken care of by one of the methods previously mentioned. The dorsal or the palmar surface or both may be thus covered with whole thickness skin with its subcutaneous tissue, and by this means a functionally useful hand may be developed from what was previously a painful claw.

#### TREATMENT FOR WEBBED TOES

It is seldom necessary to operate for relief from webbed toes, as this deformity, if incomplete, causes little if any disturbance of growth or function. However, if there is complete fusion of the terminal phalanges of toes of unequal length, such as the second and third, it is essential that these toes be separated sufficiently to allow unhindered individual growth. If this is not done early, the added deformity due to unequal growth will cause the longer toe to assume somewhat the position of a hammer toe, and in time considerable loss of function will follow, there will also be difficulty in getting a comfortable shoe. When such fusion exists, the terminal phalanges should be separated in the midline as soon as the unequal growth becomes evident, and the raw surfaces should be grafted with a whole thickness skin graft. This procedure is usually sufficient to control the situation, and we have never felt it necessary to separate the toes completely and attempt the formation of a new commissure on the normal level.

#### COMMENTS

As in any other plastic operation, tension must be avoided, and it is better to graft a raw surface than to attempt to suture edges of skin or flaps under tension. By the proper use of skin grafts, harmful tension may be absolutely eliminated. Primary healing is essential, as excessive scar formation may cause secondary deformity. We prefer grafts of whole thickness skin to any other type when dealing with raw surfaces in cases of syndactylism, as the ultimate results are much more satisfactory than when thin Ollier-Thiersch grafts or half thickness grafts are used. It is poor judgment to use the smaller types of grafts for covering raw surfaces in these cases as the scar tissue subsequently formed will cause contracture.

In certain complicated cases, pedunculated flaps from distant parts may be used to supply skin for the commissure and also for closing raw surfaces. These flaps should ordinarily be prepared in advance by one of the methods of delayed transfer, although occasionally a gauntlet flap may be formed and used immediately. The operation of Didot, which looks so feasible in a diagram, and which is so frequently selected by the uninitiated, can seldom be utilized successfully when the fusion is close, as the skin is almost always too scant to allow the flaps to be sutured without considerable tension. It is possible that some of the cases of gangrene of the terminal phalanges that have been reported may be due to too much tension in the closing of these flaps rather than to an abnormal arrangement of the blood supply.

When several fingers are fused, it is advisable to separate only two of them on the same hand at one time, as the amount of skin available is usually scanty, and if more than two are done the circulation of all may be jeopardized.

When closely fused fingers are separated, gangrene of the flaps and even of the terminal phalanges of one or both fingers occasionally occurs. Unless the underlying tissues are divided exactly in the midline, important vessels which normally adequately supply both fingers may be cut, and when the flaps are sutured, possibly under tension the remaining blood supply is insufficient to nourish the part. Occasionally the blood supply of fused fingers is congenitally abnormal, and while it is sufficient to nourish both fingers when together after separation takes place it may fail to take care of either one or both.

Fused phalangeal bones should be separated with a thin bladed osteotome, and the separation should be as even as possible in order to preserve the symmetry of the fingers. When chiseling is necessary, it is seldom if ever possible to make a skin closure by suture, so that skin must be grafted over the raw surface of the bone. There is often a tendency for the terminal phalanges that have been fused and separated, to tilt sometimes toward the normal side and sometimes toward the grafted or sutured side. The tilting of the terminal phalanx toward the normal side is probably caused by changes in the shape of the joint due to hindrance to proper development and to the weakness or lack of lateral joint ligaments. The scar contracture of the sutured or grafted side is often unable to overcome this tilting. The tilting toward the sutured or grafted side of finger can be easily accounted for by scar contracture, but in some cases hindered development and joint change are also present.

Massage and passive motion, with proper splinting, may overcome this tilting in time. If it cannot be corrected by these simple means and the deformity is objectionable, some operative procedure such as the excision of the contracted scar followed by grafting or the use of a

flap may be helpful. Should this be unsuccessful, osteotomy or the relaxation of the lateral joint ligaments may be indicated.

#### SUMMARY

Webbing of the fingers or toes either may be a congenital developmental defect or may be acquired. In the congenital type, there may or may not be a family history of similar malformations. The acquired type usually follows severe trauma or burns.

The fusion varies in degree from a slight lengthening of the normal web to complete coherence of the digits. Many operative procedures have been devised for the cure of syndactylism, but no single operation can be used successfully for all degrees of webbing.

In congenital cases, we have found that we can eliminate considerable deformity by the early separation of completely fused fingers of unequal length far enough back to allow unhindered individual digital growth, this is difficult to correct subsequently. The separation should be made as soon as the inequality of growth becomes apparent, however young the child may be, and skin should be grafted over the raw surfaces.

We have also found it advisable not to separate the fingers completely and reconstruct the new commissure until the child is at least 6 years old, as the work will have to be repeated in the majority of cases if it is done too early.

The key to final success in both the congenital and the acquired types of deformity is the formation of a satisfactory commissure, and this may best be accomplished by the use of either flaps or whole thickness grafts, depending on conditions.

The skin should be sutured over the raw surfaces left after separation of the fingers, if it is sufficiently lax to be closed without undue tension, otherwise a graft of whole thickness skin should be used. We feel that the use of whole thickness grafts for covering the raw surfaces and also for forming the commissure, is the method of choice in many instances, as by this procedure the problem of complicated flaps and undue tension can be avoided.



# SURGICAL WOUNDS IN HUMAN BEINGS

## A HISTOLOGIC STUDY OF HEALING WITH PRACTICAL APPLICATIONS TO FIBROUS HEALING\*

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Rational management of surgical wounds demands that the surgeon possess accurate knowledge of the processes of repair in tissues in human beings. The knowledge of healing of wounds in human beings is drawn largely by analogy from the observations of wounds in laboratory animals. Since the processes observed in wounds in human beings differ from those observed in tissues of animals, it is necessary to review the process of healing as found in the former.

In the first study it was observed that there are two distinct types of healing processes, an epithelial and a fibrous process. Epithelial healing has been described. This paper deals with the fibrous type which is common to the dermis, fat, fascia and muscle. The observations and conclusions made are of direct clinical value.

### STUDY OF CELLULAR MECHANICS IN FIBROUS HEALING

The material for this work consists of complete, transverse sections of surgical wounds in human beings both clean and infected in all stages of healing. Eighty-nine wounds from one day to nine years old, were studied.

Both the literature and the histologic observations on the healing of wounds are practically interchangeable with the literature and observations on inflammation. In both processes the most striking histologic picture is caused, not by fibroblasts, as they are ordinarily known but by so-called exudate cells which appear in the tissues. Both processes result in terminal fibrosis. Many writers assign the function of phagocytosis of tissue debris to the exudate cells. Only a few suggest that the exudate cells help to form the newly deposited fibrous tissue. The origin, function and destination of the exudate cells form the basis and major part of the literature on the healing of wounds. These cells have many different names and descriptions. Clasmatocytes, macrophages, polyblasts, histiocytes and endothelial leukocytes are but a few of the names. I shall call them macrophages.

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† Submitted for publication, May 29, 1929.

\* Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the Degree of Doctor of Philosophy in Surgery.

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There are three schools of opinion concerning the source of exudate cells. Perhaps the opinion most widely accepted in this country is that of Mallory and his co-workers, that macrophages are derived from the endothelium of the vascular tree and organs. A second opinion is that the exudate cells arise either by division or by "dedifferentiation" of tissue cells which become "embryonic fibroblasts." A third conception was inaugurated by Cohnheim, who believed that the exudate cells were leukocytes. Maximow<sup>1</sup> and his co-workers<sup>2</sup> have kept alive this idea, and they and other investigators by means of tissue cultures of adult lymphocytes and mononucleated leukocytes, have recently substantiated this view. There is no doubt now that lymphocytes, *in vitro*, will develop rapidly into typical macrophages, and even into typical fibroblasts which differ in no way from the macrophages and fibroblasts cultured from fibrous tissue.<sup>3</sup> Such cultures of blood cells recently have been observed to produce fibrous material resembling collagen in every respect.<sup>4</sup>

Although organic in nature, collagen fibers are apparently inanimate structures. No one has actually observed the formation of a collagen fiber in the body. Hence there are numerous opinions as to their method of formation, of which the three most important are (1) that they are formed intracellularly by fibroblasts and cast out, (2) that they are formed in the ectoplasm of fibroblasts and cast off and (3) that they are formed extracellularly. Whatever their source, from the surgical standpoint (the production of permanent tissue union) the fibers are the most important part of the process of healing. They provide for the union of severed tissues. They allow resumption of function in skin, fascia and muscle, and even in bone. They produce

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1 Maximow, A. A. Development of Non-Granular Leukocytes (Lymphocytes and Monocytes) into Polyblasts (Macrophages) and Fibroblasts *in Vitro*, *Proc Soc Exper Biol & Med* **24** 570, 1927

2 Bloom, William. Transformation of Lymphocytes of Thoracic Duct into Polyblasts (Macrophages) in Tissue Culture, *Proc Soc Exper Biol & Med* **24** 567, 1927. Carrel, Alexis. Growth-Promoting Function of Leucocytes, *J Exper Med* **36** 385 1922.

3 Carrel, Alexis. Tissue Culture and Cell Physiology, *Physiol Rev* **4** 1, 1924. Carrel, Alexis and Ebeling, A. H. Pure Cultures of Large Mononuclear Leucocytes, *J Exper Med* **36** 365, 1922. Foot, N. C. The Endothelial Phagocyte. A Critical Review, *Anat Rec* **30** 15, 1925. Maximoff, A. De l'action stimulante de l'extrait de moelle osseuse sur la croissance et l'évolution des cellules dans les cultures de tissu lymphoïde, *Compt rend Soc de biol* **80** 225 1917. Maximow, A. The Cultivation of Connective Tissue of Adult Mammals *in Vitro*, *Arch Russ d'anat d'hist et d'embryol* **1** 105 1916.

4 Ebeling, A. H., and Fischer, A. Mixed Cultures of Pure Strains of Fibroblasts and Epithelial Cells, *J Exper Med* **36** 285 1922. Maximow, Alexander. Development of Argvrophile and Collagenous Fibers in Tissue Cultures. *Proc Soc Exper Biol & Med* **25** 439 1928.

the abnormalities of wounds. Whatever cells, if any, are required to produce them are subservient to them and are primary only in the order of time.

Some writers have endowed the fibers of inflammatory or healing tissue with the ability to move independently and to direct their motion. In wounds in human beings the rapidity with which a mass of disarranged newly formed fibers becomes aligned and organized into a tissue might be regarded as substantiating evidence for such a conception. There is no evidence in wounds in human beings, however, that such powers exist in the collagen fibers of dermis or fascia.

It is commonly believed that fibroblasts produce the healing fibrous material only after the macrophages have cleared away tissue debris and thus have prepared the field for the cells present in the region to build new tissue. The succeeding observations of wounds in human beings show that: (1) there is no healing outgrowth of fibroblasts or fibers from the fascia or dermis; (2) the healing cicatrix is formed by the exudate cells, or the macrophages; (3) fat, instead of being a tissue inert in or inimical to the healing process, is of great importance in the furtherance of healing; (4) the determination of the healing fibrosis is directly related to physical forces; and (5) the blood lymphocyte apparently is the true healing cell, acting as both macrophage and fibroblast. All of these observations are of clinical significance.

*Healing of the Dermis*—Throughout the study of the eighty-nine wounds in the series certain features occurred frequently enough to justify general statements. The cut ends of the dermis remain inert. In wounds that are from one to thirty days old, regardless of the degree of healing, the cut margins of the dermis stand out as distinct lines. Nowhere is there evidence of any reaction of growth in the dermis itself. The resident tissue cells are not massed in greater than normal numbers near the margin of the wound, those that are present are not immoderately enlarged or dedifferentiated and mitosis or other evidences of cellular proliferation are extremely uncommon. The exposed fibers do not change either in form or in number. The only definite reaction appearing in the dermis itself is a slight increase in the so-called round cell infiltration in the interstices about sweat glands and small vessels, yet the dermis is united rapidly by the formation of new fibrous tissue between its cut margins. Although in older wounds this interposed, uniting, fibrous tissue is intimately connected with the margins of the old dermis, in the earlier stages of its formation there is no arrangement of its cells or fibers to indicate its origin from the edges of the dermis. From these facts it must be concluded that the cells and fibers of the dermis do not take a part in the production of the healing cicatrix, and that the new scar tissue must therefore develop from cells not normally present in the dermis (fig. 1).

The new healing tissue between the edges of the dermis lies in the fat between, or immediately subjacent to, these edges. In wounds from four to thirty days old, this new tissue may be divided into three zones: (1) a cellular zone composed of macrophages, (2) an acellular zone of new fibers, and (3) a transitional or fibrocellular zone. These zones blend one with another. The cellular zone lies at the periphery of the cicatricial tissue and infiltrates the surrounding fat.



Fig 1—Dermal ends and fat in a wound four days old, in a human being. There are visible, distinct ends of old dermis, and new fibers between dermal ends. The relation of cellular infiltration to fat and the general direction of new fibers in new tissue between dermal ends are seen,  $\times 18$ .

The fibrous zone lies more directly in the plane of the preformed dermis. The fibrocellular zone provides the transition between the cells and the fibrous material which is practically free of cells. The entire process takes place in the subcutaneous fat. There was not any evidence in any wound of the formation of new fibrous tissue without a cor-

responding macrophagic reaction in the surrounding fat. In a few wounds that did not show reaction in the fat there was absolutely no evidence of fibrous healing. This is an important observation, for fat as a tissue is generally considered to contribute nothing to, or even to be inimical to the process of fibrous tissue union (fig 2).

In these wounds in human beings new fibrous material is found much more intimately related to the normally nonresident exudate cells (macrophages) which infiltrate the fat than to the cells or fibers of the preformed functioning, fibrous dermis. Since evidence is not found

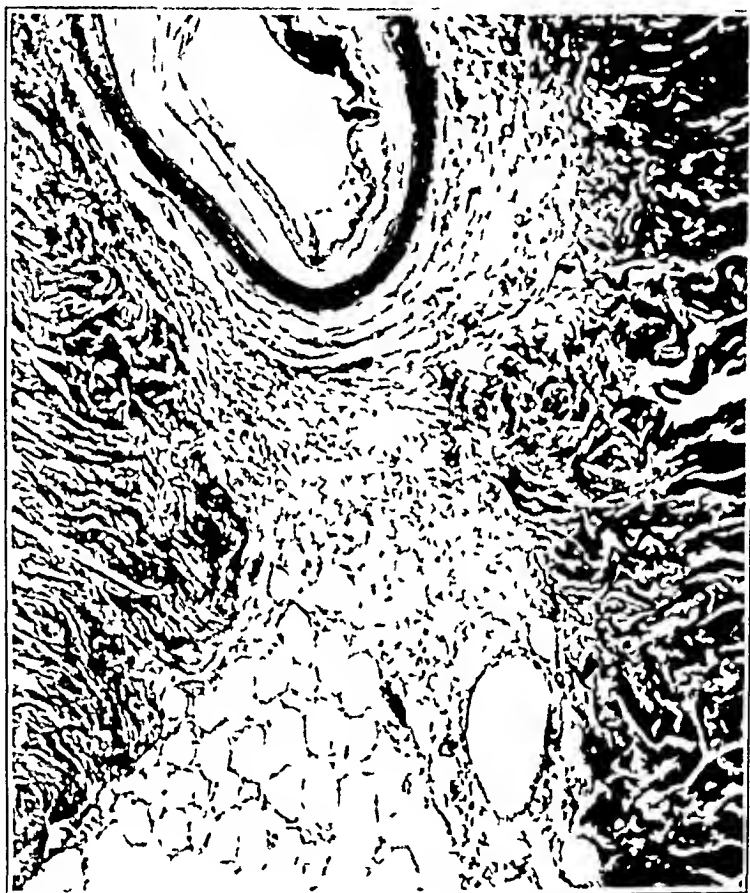


Fig 2—The healing of the dermis in a wound seventeen days old in a human being. There is no evidence of outgrowth of tissue from dermal ends. The cellular (macrophagic) zone in fat and the fibrocellular and fibrous zones with direct transitions, are seen,  $\times 75$ .

which points to increased activity of the normally resident fibroblasts, it must be concluded that, if the fibers are formed by cells they are formed by the macrophages with which they are so intimately related. The three zones of the process—the cellular or macrophagic, the fibrocellular and the fibrous zones in a given wound—may therefore be considered as sequential stages of the process of production of fibers. As all three stages are found in any healing wound which is from

four to thirty days old, it must be concluded that the age of the wound alone does not determine the histologic picture of the wound

*Healing of the Fascia*—The same features are observed between healing fascial margins. The fascia does not present indication of rapid dedifferentiation, of multiplication, or of growth or movement of its cells or fibers into the wound from its cut margins. Scar tissue, however, forms between the severed fascial structures. Here again it must be concluded that the cells and fibers of the fascial structures do not take an active part in the formation of the healing cicatrix. As in the dermis, so in the fascia, the only visible reaction of healing is found in the fatty tissue interposed between the fascial margins or adjacent to them. Likewise, there are three zones of the healing tissue: the cellular zone, the fibrous zone and the transitional fibrocellular zone. Also, as in the dermis, the macrophagic zone infiltrates the fat, whereas the site of the most advanced fibrosis is in the fascial plane. Remnants of fat cells within the fibrocellular and fibrous zones, in both the planes of dermis and those of fascia, indicate that the entire healing process takes place in fat. To some extent, injured muscle may be the site of the healing process of fascia. When this happens, however, the muscle fibers atrophy and the stroma of the muscle takes on the appearance of fatty tissue. The macrophages then infiltrate the spaces in the stroma of the muscle which assumes the appearance of infiltrated fat. In much of the injured muscle there is gross and microscopic evidence either of a transition to fat or of a deposition of fat in the stroma (fig 3).

*The Organization of the Healing Fibers*—The earliest fibers of scar tissue are found in the transitional, fibrocellular zone of the healing process. Here the fibers are never very long, are often thin and wavy and do not show evidence of organization into bundles. They are not adherent one to the other, nor are their axes parallel. Such scar tissue is patently unable to function properly as a uniting substance capable of withstanding the stresses and strains put on dermis and fascia in daily life. To be a functioning tissue this new fibrous material must be organized. Evidence of organization is found in the fibrous zone of the process, where the cells have disappeared and the fibers are agglutinated or clumped into heavier, straighter bundles the axes of which are more or less parallel to each other and to the planes of the fascial structures in which they lie.

As has been noted the most advanced transformation of the healing material into fibrous tissue lies always in the planes of the dermis and fascia. This observation is of great interest. Something other than the age of the wound and something related to such fascial planes must determine this mode of healing. The cut ends of the pictorial structures do not determine it for in the case of fascia they are more

often than not turned back from the line of the incision by the pull of the sutures so that they lie entirely out of the general fascial plane (fig 4). The sole function of all fibrous tissue in the body is the bearing of stress and strain. Fascia and dermis are organized to bear linear forces in given planes. The suturing of fascia and dermis results in the maintenance of this function at and across the line of the incision. Naturally, stresses will be transmitted through the healing material in the general plane of the fascial structure. The occurrence of the most advanced stage of fibrous deposit and organization in the planes of the dermis and fascia, therefore, can be related to the functions of these

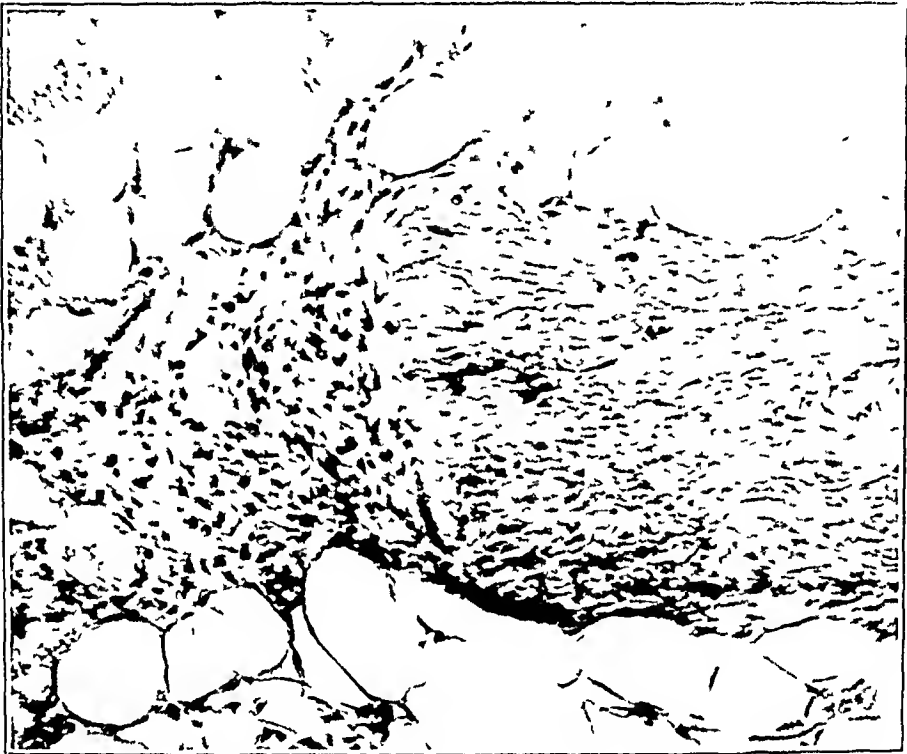


Fig 3—The healing of fascia in a wound eleven days old. There is no evidence of outgrowth of tissue from the fascial end. The cellular (macrophagic and lymphocytic) infiltration in fat at the fascial end and dilated capillaries bordering the infiltration are seen,  $\times 170$ .

structures and to the transmission of linear stresses across the line of incision in the general planes of these structures.

The alinement of the fibers and their organization into a functioning tissue structure I consider to be the response of the new scar tissue to linear forces. The direction of the fibers of muscle tendons and aponeuroses throughout the body, and of the trabeculae in the bone, is but the normal expression of such a response. The disappearance of the healing cells fits directly into the mechanical economy of the process, for their presence would not add tensile strength to the new

tissue, on the other hand, it would tend to reduce tensile strength by separation of the bundles of fibers

The principle of the alinement of fibers along the lines of physical forces is perhaps best illustrated in both normal and regenerating bone, in which, as is well known, the ultimate directions of the trabeculae are directly dependent on the directions of the lines of force exerted through the bone. In fact, the whole process of healing fibrosis may be compared to the repair of bone. The bone itself, the functioning structure, does not grow out from the fractured ends. The functioning structure, however, is quickly united by a deposit of scar tissue created by cells and fibers which formerly did not take a part in the normal supportive function of the bone. This fibrous mass is ossified and



Fig 4—The block from which sections were cut from a wound ten days old, in a human being. Skin, fat, fascia, muscle and peritoneum are seen. The fascial ends are forced away from the line of incision by the tension of the sutures (actual size)

gradually reorganized according to principles mathematically and architecturally correct which relate to the sustaining of stress and strain. Fibrous healing is identical except for the lack of ossification. Even this was present in two of the abdominal wounds studied, although the wounds were not related to any bone or cartilage. The comparison is still more marked in the light of Macklin's<sup>5</sup> work on the repair of bone which, with recent observations on tissue culture, implicates macrophages as the source of the primary fibrous callus in the repair of bone.

<sup>5</sup> Macklin, C. C. The Development and Function of Macrophages in the Repair of Experimental Bone-Wounds in Rats Vitrally Stained with Trypan-Blue, Carnegie Institute Contributions to Embryology 9 3 1920



In the reorganization of ossified material certain cells appear to destroy or to build bone according to lines of force that can be projected through the substance. The alignment of the resulting trabeculae is therefore dependent on the activities of cells. It is possible that fibroblasts or macrophages may, by a response to linear forces projected through new scar tissue, move through it in such a manner that they agglutinate and align the fibers in the direction of the stresses which



Fig. 5—Fibers and macrophages in fat of a wound, ten days old, in a human being. The relation of new fibers to macrophages is evident. Lymphocytes, macrophages and intermediate forms are present.  $\times 450$

the new tissue bears. The remarkable disappearance of the fiber-forming cells concomitant with the appearance and organization of new fibrous tissue, however, cannot be assigned completely to an emigration of the cells.

*The Origin of the Healing Fibrosis*—Low-power microscopic fields show the apparent transition of masses of macrophages into organized connective tissue containing few cells. High-power fields reveal the

direct transition of both intracellular and extracellular cytoplasm of macrophages into fibers (figs 5 and 6). In some cases this transition appears to be the result of a streaming out of the cytoplasm behind a moving cell. As the macrophages appear to form the new fibers, and as the cells normally resident in the connective tissue appear to take no part in the production of the healing tissue, one may well question: What is a fibroblast? In wounds in human beings it is evident that the macrophage is the true fibroblast. New fibers are

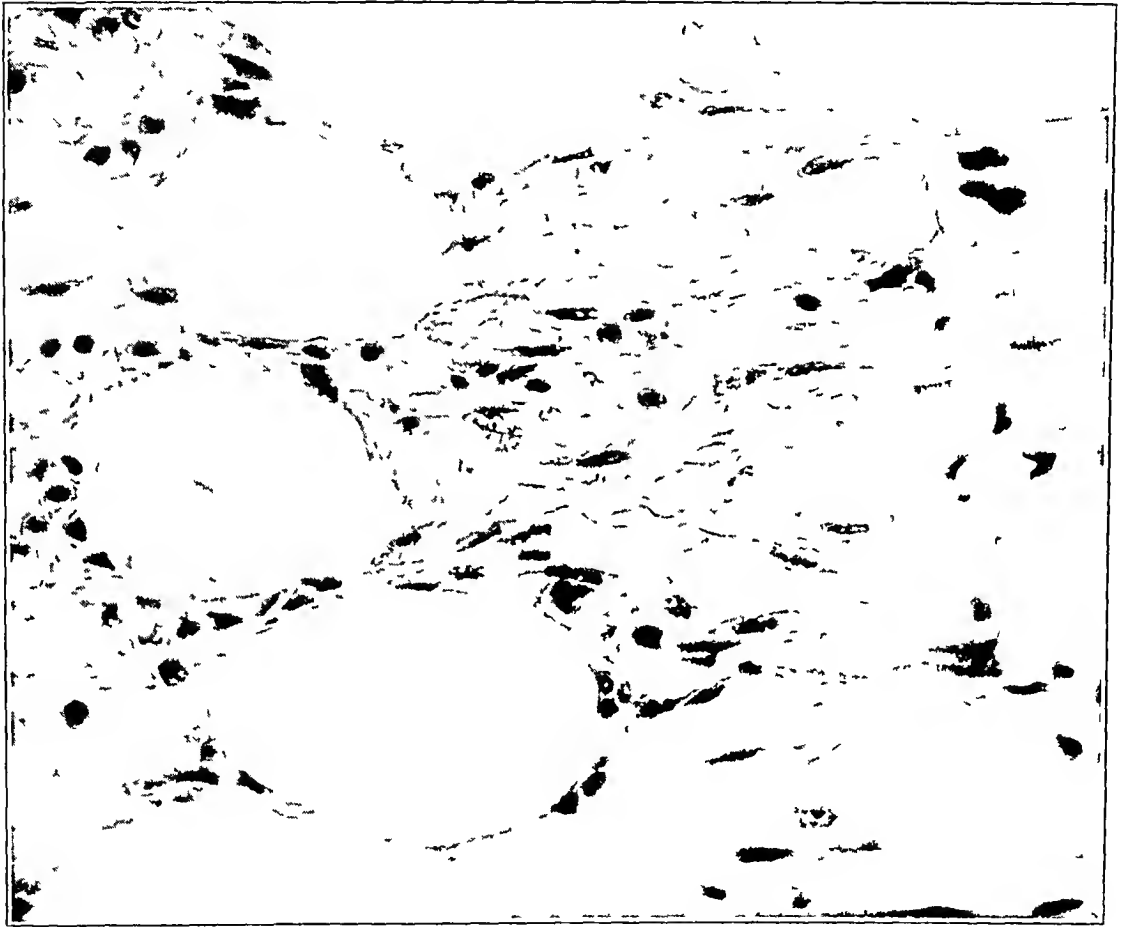


Fig. 6—Fibers and macrophages in fat of a wound ten days old in a human being. Some fibers are related to cellular cytoplasm; other fibers are not related to any cells or cytoplasm. Fat has been replaced by cells and fibers. Transitional forms between lymphocytes, on the one hand, and macrophages and fibroblasts, on the other hand, are seen.  $\times 450$

found chiefly among macrophages, and masses of macrophages are replaced by practically acellular fibrous tissue. Definite indication of the disintegration of the macrophages is concomitant with the appearance of a large number of fibers among them. New fibers are found as part of the strung-out cytoplasm of macrophages, as partially intracellular and partially extracellular fibrils, and as totally extracellular

objects formed from some material present in the intercellular spaces. Occasionally new fibers of collagen may be traced directly into fibers of fibrin. Certain it is that as fibrosis progresses the cells disappear, chiefly by disintegration. A few of the macrophages appear to take on the cytologic characteristics of ordinary tissue fibroblasts. From these observations it appears that the determination of new fibrous tissue is dependent on two factors: (1) the presence of a chemical substance in the healing zone which can be changed quickly into collagen fibers, and (2) the passage of physical forces through the healing material. The macrophages appear to provide the necessary chemical basis for the fibers. The material is set free for coagulation into fibrils, and the field is freed for the most economical organization of the fibrils by means of the rapid disintegration of the macrophages.

*The Origin of the Macrophages or Round Fibroblasts*—In these wounds in human beings it is obvious that macrophages are not derived from the fibroblasts normally present in the preformed tissue. If they are endothelial cells, as many believe them to be, they are unlike true endothelial cells which line the vessels of the region. Their residence is fat. Normally, in fat there are no cell forms from which such a large number of cells might spring in such a short time, and there are but rarely any evidences of the multiplication of cells. The exudate cells or macrophages must be derived from cells which come to the region of the wound from elsewhere in the body. Among the macrophages are many cells identical with lymphocytes of the blood. Many of the larger macrophages have nuclei almost identical with the small compact nuclei of lymphocytes (fig 7). Indeed transitional forms between lymphocytes and macrophages are everywhere to be found. Lymphocytes are found abundantly as perivascular infiltrates about dilated veins and capillaries and within the vessels of the region in numbers greater than normal. The lymphocyte is known to be a motile cell, and to be capable of rapid growth into macrophagic form *in vitro*. It may be concluded then, that the lymphocyte of the blood is the cell which originally infiltrates the fat of the region of the wound, and that the macrophage is derived from the lymphocyte by a process of growth. Thus the lymphocyte becomes the real fibroblast in healing of the wound. Such a fibroblastic rôle for the lymphocyte has long been accepted by the French because of the constant occurrence of lymphocytes in chronic inflammatory connective tissue.

*The Rôle of Fat in the Process of Healing*—Fat is the place where the healing process occurs, and lymphocytes are the primary infiltrating cells, which by their growth become macrophages. The infiltrating cells do not merely push aside the fat cells as they enlarge to become macrophages. The fat cells are replaced by the growing cells, which take on a greatly swollen and foamy appearance as the fat cells diminish.

in size. Fat stains show that the infiltrating cells are packed with fat. It must be concluded, then, that the growth of the infiltrating lymphocytes is due directly to the ingestion of the fat in which they lie.

The histologic picture of macrophages in fat has been described by many authorities as indicative of a development of new fat cells; the macrophages are assumed to be young fat cells with their content of fat still in droplet form. In wounds in human beings, however, such a picture is the exact opposite of that of the generation of fat



Fig 7—Fat with typical infiltration of macrophages and lymphocytes in a wound seven days old, in a human being. Lymphocytes, macrophages and all intermediate transitional stages are present. There is replacement of fat cells by the infiltrate,  $\times 120$ .

It is the picture of replacement of fat. This interpretation is completely substantiated by the histologic picture of progressive lipodystrophy, in which disease the subcutaneous fat is completely replaced by sclerotic fibrous tissue; the histologic phases of the process are absolutely interchangeable with those found in wounds of human beings.

It already has been noted that the healing fibrosis takes place in fat, now it appears that fat is the food for the healing cells. These

conclusions are at direct variance with the clinical impression that subcutaneous fat, as a tissue, serves only as unavoidable debris in surgical incisions. Since the final fibrous material is largely deposited by the disintegration of the healing cells, and since the healing cells live chiefly on fat it may be further concluded that the subcutaneous fat serves as the chemical basis for the healing fibers. Adipose tissue therefore serves as an emergency food depot for healing cells. Such a conclusion is substantiated by the fact that fat is the food of the cells of the embryo. Maximow<sup>6</sup> and Carrel<sup>7</sup> have shown that lymphocytes act as embryonic cells. Such a conception of fat as a food depot for emergency repair of tissue suggests an explanation for the widespread distribution of fat in the body, particularly along fibrous structures subject to trauma, such as the skin and fascial sheaths. Fatty tissue is not present within the central nervous system where true fibrous tissue does not form after injury.

*The Healing of Fat as a Tissue*—The healing process which unites fascia and dermis takes place in fat. In the healing of fat itself the infiltrating cells are scattered along the line of incision, extending laterally between fat cells and fat lobules or invading the fat cells themselves. Then growth into macrophages and the deposit of fibers by their disintegration are as described for fibrous structures. The chief site of new fibrous tissue in fat is along the small fibrous trabeculae which course through the fat; this fact again impresses one with the relation between healing fibrosis and structures that transmit tension. In old, long healed wounds no evidence of healing fibrosis may be found in the fat, indicating that absorption follows the process of fibrosis when it takes place in regions the function of which is not to bear permanent stress.

*Healing of Muscle*—Muscle is healed by an increase of macrophages at the injured area. The muscle fibers atrophy or retract from their connective tissue stroma. The stroma becomes packed with lymphocytes, macrophages and intermediate forms, all of which disappear as fibrosis occurs. The fibrous deposit unites the stroma of the muscle on one side of the incision to that on the other side, thus assuring maintenance of the function of the muscles at the part. As the healing process is continuous throughout the wound, it is not surprising that structures such as skin and muscle, or fascia and muscle, which normally are separated, may become adherent (fig. 8).

*Healing of the Peritoneum*—The healing of the fibrous portion of the peritoneum is included in the description of fascial healing. No true, serosal, lining cell layer was observed in any of the wounds.

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6 Maximow (footnote 3, fifth reference)

7 Carrel (footnote 2, second reference)

examined. It may have been lost in the process of preparing the tissues. Any conception of the action of such cells is not permissible from this study.

*Healing by Primary and Secondary Intention*—The observations given apply alike to "clean" and to infected wounds. Any single wound may be partly clean and partly infected. In wounds of human

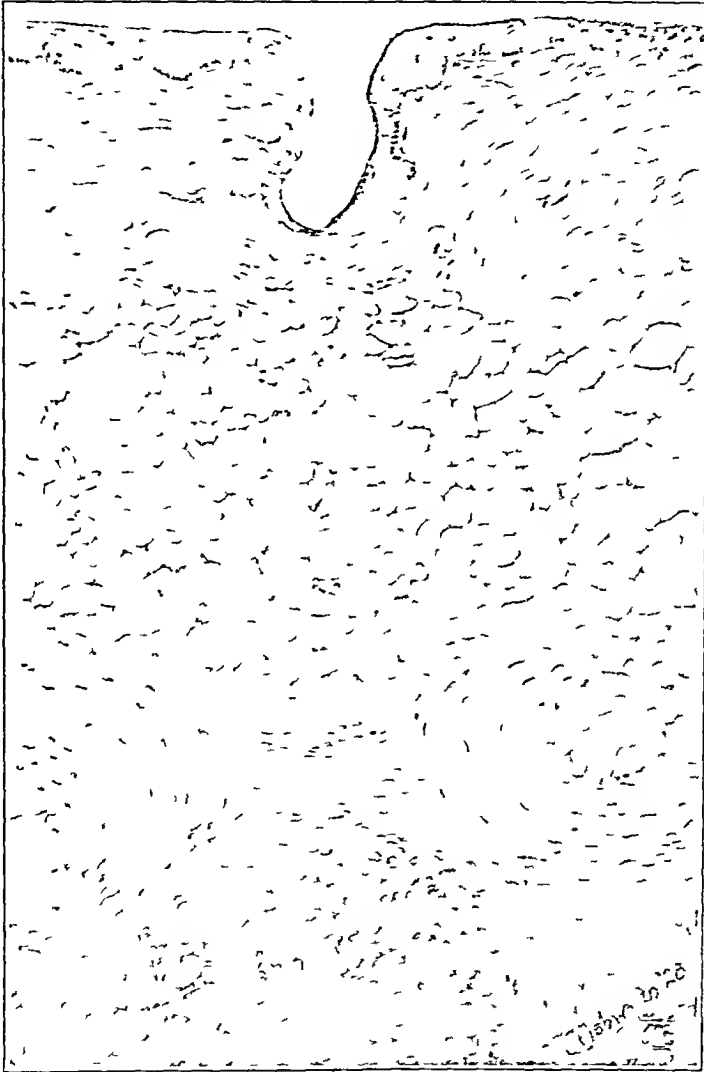


Fig 8—Diagrammatic drawing of a wound ten days old. Epithelium dips into the wound over inert dermal ends. Both dermal and fascial ends do not show increase in or outgrowth of cells. There are three zones of healing in the same wound, fibrous in planes of fascia and dermis, cellular in fat, and fibrocellular between these zones. Macrophages have infiltrated the muscle, and macrophages and fibers have replaced fat. There is no granulation tissue. The dermis has healed across the lowest part of the dermal incision.

beings, granulation tissue is seldom found, even though there is evidence of infection in the field. When present it is always on a surface

either superficially as in a sinus or lining a space deep in the tissues. Even in typical granulation tissue the types of cells present substantiate the conception that the lymphocyte and macrophage are the healing cells. Granulation tissue must be regarded as a vascular overgrowth into an open space by means of which the healing cells are brought into the space and in the absence of fat supplied with nourishment from the blood until they are present in sufficient numbers and have developed sufficiently to produce the fibrous material which will not only obliterate the cavity but which will produce a stress-resistant tissue in the space. It is merely a vascular phase of the fundamental type of healing process and is related to infection only because it is in infected wounds that spaces within the tissues most frequently develop and because surface wounds are invariably contaminated. Primary and secondary intention therefore represent but two phases of one fundamental healing process and healing is primarily the same in both clean and infected wounds.

*Wound Debris and the 'Latent Period' of Healing*—The idea that macrophages do more than simply act as scavengers of "tissue debris" is one not generally accepted. In fact the term debris has been applied to the normal exudative products of inflammation and to normal fat as well as to injured or useless tissue. In wounds in human beings degenerated tissue is not found in an amount sufficient to account for the number of macrophages that appear. It is suggested by this fact and by the part played by the "scavenger" macrophage cells in producing fibrous deposit, that the term debris is improperly used in this connection. It appears that the exudative products in the healing of wounds and what injured tissue there may be possess a direct contributory function in the healing process as food for the healing cells and then as constituents of the fibers which are deposited. In other words, healing begins at once and there is no period of degeneration or of dedifferentiation preceding the period of regeneration.

*The Process of Healing of Wounds as Related to Function of Severed Tissues*—Since Virchow and the discovery of mitosis the tendency has been to consider it but logical that new tissue must be derived directly from old tissue of the same kind. The rapid derivation of new tissue from dermis or fascia, however, would create great changes in those tissues through cellular proliferation and movements or by so-called dedifferentiation of the tissue. Such changes would tend to separate the fibers and thereby to weaken the tissue and jeopardize the normal function of the structure. If that function is ever important, it must be more so when the continuity of the part has been destroyed by surgical incision. Furthermore in surgical wounds,

an added function falls on the immediate ends of the severed fibrous structures. On them falls the strain transmitted by the sutures when the wound is closed. Increased cellularity of such fascial ends with resultant swelling of the fascia and consequent separation of the fibers would make the suturing of fascia or dermis a procedure of doubtful value, for sutures would tear out easily. Fascial suturing is however the main source of strength in the closure of wounds. To make this true, the strength of the fascia in wounds of human beings is maintained by minimal changes from the normal structure of the tissue.

Considering the necessity for the maintenance of normal function of the preformed tissues it does not seem illogical, in spite of the belief inaugurated by Nichow, that new connective tissue should be derived in some manner not necessitating changes in structure of local tissues. When the economy of the organism is considered the inauguration of healing fibrosis through the medium of infiltrating lymphocytes, the growth of the lymphocytes by the ingestion of the local, nonsupportive fat and the deposit of the uniting fibrous material between the margins of the supporting tissues by the lymphocytes seems a logical process.

The implication of lymphocytes in the deposit of fibrous tissue suggests that, in cases in which the healing of wounds has been delayed without apparent cause some method may be found by which the fibroblastic potentialities of the lymphocytes of the blood may be stimulated.

*Controls*—As controls for this work, 101 experimental surgical incisions in animals were studied. As in the wounds in human beings the cells and fibers of fascia and dermis do not show evidences of proliferations or movement into the wound. From this point on, the observations in the animals do not correspond with those in the human material. In the guinea-pig, rabbit and dog, granulation tissue is responsible for by far the most common picture of healing even in apparently clean wounds. In swine as in human beings, granulation tissue is rarely seen. This difference is accounted for by the character of the subcutaneous tissues in the various subjects. In the smaller animals, the subdermic tissue is largely areolar tissue, this is a potential space which, if edema is present, becomes filled with fluid. In swine and in human beings this space is occupied by compact adipose tissue which can be directly ingested by macrophages hence granulation tissue is not formed.

In animals, the origin of the healing cells is not clear. Mitosis is common which suggests that the healing cells are of local origin. The form of these cells also more nearly resembles that of swollen tissue fibroblasts. Nevertheless transition forms from lymphocytes



to small macrophages and fibroblasts also are present and the larger cells contain many fat-staining globules. Masses of macrophages such as occur universally in wounds of human beings do not appear in the animal tissues. There is a distinct difference between the histologic picture of healing in animals as compared to healing in human beings. This difference emphasizes the fact that the conception of healing in surgical wounds of human beings must be built up from observations on human tissues.

#### CLINICAL APPLICATIONS

The concept of healing in wounds that has been explained in the foregoing paragraphs finds direct application to several well established clinical facts and surgical procedures and throws doubt on some clinical impressions.

*Fat in Surgery*—There is a paradox in the attitude of surgeons toward fat as a tissue. They distrust subcutaneous fat because of its poor ability to resist trauma and its tendency to become infected and to interfere with the healing of wounds. At the same time surgeons, as a routine measure, sew omental fat over intestinal suture lines to support them and to aid healing, in spite of the fact that such places present the greatest possible likelihood of contamination and fat the least possible supportive strength. There is no demonstrable difference histologically between the two types of fat and Mann<sup>8</sup> has shown experimentally that subcutaneous fat may be substituted for omental fat in technical procedures with as good results as though omental fat were used.

The observations presented in this paper show definitely that subcutaneous fat serves as the place in which the healing process occurs and as the source of nourishment for the cells that take part in it. On this twofold function of fat is based the healing of parietal incisions. Therein also must lie the value of fat of any sort when placed about intestinal suture lines.

The common opinion that subcutaneous fat acts as a deterrent to proper healing must be explained on some basis other than that the fat tissue itself is the deterrent.

*An Explanation of the Broad Scar of a "Knife-line" Incision*—It is common knowledge that, after ordinary over-and-over suturing an epithelial scar, which ten days after the incision is well healed and of the "knife-line" type may be a broad and irregular scar ten months later. On the other hand, the wound that is closed with closely placed mattress sutures so as to evict both margins of the skin may not look

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<sup>8</sup> Mann, F. C. The Transplantation of Fat in the Peritoneal Cavity. *S. Clin. North America* 1: 1465, 1921.

well before the stitches are removed, yet may be barely visible after ten months. The studies reported here show that the healing of skin occurs through the interposed or subjacent fatty tissue. On transverse section, the incision in the skin is found to be a deep crevice in the dermis, the bottom of which is formed by new fibrous tissue in the fat. The parts of the dermal margins that protrude above the bottom of the crevice will be lost to the function of the dermis, as the lines of force exerted across the line of incision through the general plane of the skin, will pass beneath them. Gradually, then, these upright dermal margins disappear, either by being retracted laterally into the general plane of function, or by being absorbed. In either case, there is flattening out and exposure of the rather extensive scar epithelium which had dipped into the depths of the dermal wound, and rearrangement of the epithelium about the incision line, which results in the ultimate scar on the surface being a wide scar instead of a narrow line.

In wounds closed with everted edges, the interdermic scar tissue is also formed with the help of the fat. In this case the fat unites the approximated under surfaces of the dermal margins for some distance back from the actual dermal edges with a short length of new fibrous matter between the under surfaces. When the sutures are removed, the tension in the surrounding skin tends to pull the everted edges back into the general dermal plane. The tension is transmitted through the interposed scar, which acts as a fulcrum for the everted dermal ends, the result is that as the ends drop back into the dermal plane they are constantly forced toward each other. In this way any resorption of preformed dermis that may take place will not extend very far to either side of the incision. The end-result is, according to both gross and microscopic appearance, a very narrow "knife-line" scar.

*Fat and the Mechanics of Closure of Wounds as Related to the Causes of Postoperative Hernia*—By the described relation of physical forces to the formation and organization of fibrous tissue, the value of sutures may be explained on a basis which will permit a working explanation of the cause of postoperative hernia.

Sutures serve to unite severed fibrous structures so that they can continue their normal functions. This fact alone requires that the function of the fascia must be maintained by the sutures at and across the line of the incision during the healing of wounds. Sutures that fail, or that are formed or placed so that the stresses in the fascia or dermis cannot pass across the wound in a normal manner will be the cause of abnormal healing.

From the observations presented, it may be assumed that the beginning of a postoperative hernia occurs in a place where the continuity

of fibrous parietal structures is broken or weakened. To cause this condition sutures must have failed or must have been so placed that the functional stresses of the part are not evenly distributed across the entire wound. As a result, at that point in the closure where the normal fascial function is diminished the intra-abdominal forces exerted perpendicular to the parietal plane will exceed the tension existing in the healing tissue between the fascial margins. This may be represented diagrammatically, the length of the smaller lines representing the stresses transmitted to the fascia and across the fascial incision by the sutures.

At point *A* of figure 9, due to faulty spacing of the sutures, tension does not pass across the line of the wound in the fascial plane. This fact permits forces *B-I* which are exerted by intra-abdominal pressure and which are at right angles to the fascial plane to cause separation of the tissues. Such forces are found in the intra-abdominal tension. If by faulty suturing the area above *C-D* is puckered or relaxed

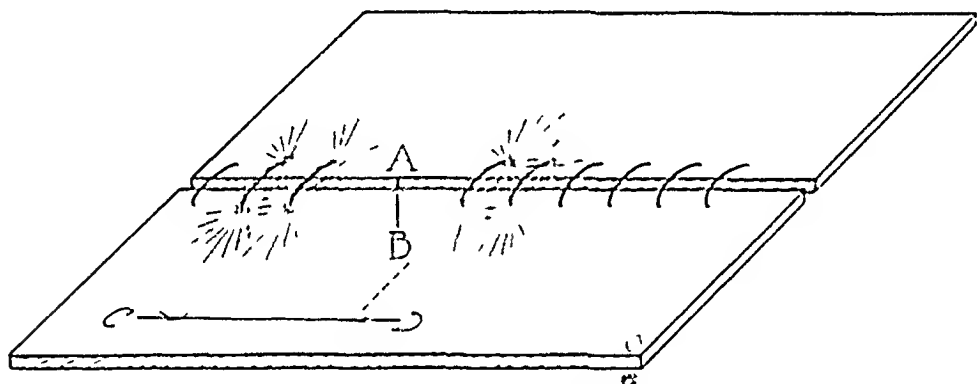


Fig. 9—Diagram of physical factors determining the healing of fascia and the formation of postoperative hernia.

parallel to the incision this will further tend to weaken the point *A* and permit greater penetration of abdominal organs into the wound. The omentum or another organ becomes interposed between the surfaces of the wound through the action of the intra-abdominal pressure on it. If there is sufficient parietal tension against the walls of this organic plug, there will be adhesion of fascia to organ providing the organ is in one position long enough to permit a fibrous union to take place, and providing both wound cavity and organ are not covered with serosal cells. If fascia at *A* is slack because of a force, *C-D*, then stress will not be transmitted at *A* and firm adhesion will not form although the penetrating organ may be stationary. The surface of the pocket in the wound is transformed by macrophages into a thin fibrous membrane which becomes a thinned out and expansible continuation of the fascial margins of the wound and forms the fibrous coat of the resulting postoperative hernia. If this fascial extension is not adherent to the penetrating viscus it becomes covered with

serosal peritoneal cells. The prevention of postoperative hernia depends therefore, largely on the proper mechanics of the fascial closure.

The objection will be made that, if histologically, fat between fascia is an aid to healing, why is it that clinically, it is a well established practice to exclude omental tags and lumps of subcutaneous fat from between fascial margins when wounds are sutured in order to prevent postoperative hernia? The answer is found in figure 9. It is corroborated by the well known tendency of the omentum to form fibrous adhesions. The fat itself is not inimical to healing fibrosis. Lumps of fat are removed from the suture line at the time of closing simply because of the difficulty of assuring proper spread of tension across the entire line of incision if any interposed mass is present between the fascial margins. The removal of the physical mass, therefore is the chief desideratum in this surgical practice. The properties of fat however make it particularly advisable to remove masses of it from the field through which tension is transmitted. It is of such a consistence that it may change its shape and slide out from between the fascial margins, or become liquefied and dispersed leaving if the healing tissue has become fairly firm, an accentuation of the condition at *A* in the diagram, a small piece of moving viscus may insinuate itself in the space that is formed. A further confirmation of the fact that it is the mass which the fat represents, and not the fat itself which must be removed from the line of fascial closure is found in the practice of overlapping fascial membranes from which it is impossible to remove all the fat. Healing in such cases takes place quickly and permanently. Full-thickness skin grafts also prove, clinically that fat as a tissue is not a hindrance to healing, and they illustrate the importance of pressure or tension in the production of fibrous tissue.

*The Closure of Wounds in Layers*—There is no doubt that the closing of wounds according to their anatomic layers procures excellent results. From this work, the explanation of the benefits of this procedure is found in the resulting maintenance of the functional planes of the fibrous structures. An explanation more commonly given is that by sewing fascia to fascia the cut ends are approximated whereby the outgrowth of fibroblasts from them is minimal and direct, and that healing is thereby accelerated. In wounds of human beings, however there is no histologic evidence that the cut ends play any part in the production of healing. Indeed the fascial ends are not only inert but they actually are turned away from each other by the pull of the sutures, as is readily observable during the closing of any fascial layer at operation. Fibrous healing is the result of a "fill" of new fibrous tissue between the severed structures and not the product of any healing outgrowth from these structures.

## CONCLUSIONS

1 Fascia and dermis do not take any active part in the healing of surgical wounds in human beings

2 Fat is the site and the basis of the production of new fibrous material in wounds of human beings

3 Macrophages are the true fibroblasts of wounds in human beings

4 New fibrous scar tissue is formed at the expense of the cells which produce it

5 Given the proper chemical material in the healing zone the physical forces in that zone determine the rate of deposit of fibrous material and the organization of the fibers into a functioning tissue

6 Macrophages are derived from lymphocytes of the blood which develop rapidly by the ingestion of fat

7 The fundamental healing process is the same in both clean and infected wounds

8 The histologic picture of fibrous healing in human beings is different from that in animals

9 The mechanics of closure of wounds determine the appearance of the scar on the surface and the occurrence of postoperative hernia

# SECONDARY OR LATE PERFORATION OF SMALL INTESTINE FROM TRAUMA

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Not infrequently the surgeon is called on to take care of the patient with abdominal injury caused by blunt force. Commensurate with its importance, this subject has been given much study, and there are many excellent articles dealing not only with certain phases of the subject, such as rupture of the spleen or liver, but also taking up the question of abdominal trauma as a whole. Demel<sup>1</sup> has recently presented such a review. In these various contributions much is said about primary rupture or perforation of the intestinal tract, but little is to be found concerning perforations that occur later when the patient is considered out of danger. I shall report two personal cases of such late perforation, supplementing them by illustrative cases from the literature, and from these data I shall endeavor to give a more or less comprehensive discussion of the condition.

## REPORT OF AUTHOR'S CASES

CASE 1—A farmer, aged 33, was admitted to the W S Major Hospital on May 22, 1926, at 2 a m, with a diagnosis of intestinal obstruction. He had become ill suddenly about midnight two days before, when he was awakened by severe pain across the midportion of the abdomen. He drove several miles to a physician's office, vomiting before arrival, two hypodermic injections of morphine were necessary to obtain relief. The next day the pain and the vomiting persisted. He had not had a bowel movement since the morning before the onset of the illness, cathartics being vomited, and an enema was unsuccessful. He had had no fever. For a year preceding, there had been an indefinite abdominal complaint at intervals as if he were going to have diarrhea. He had, however, had no treatment and no operations. Though poorly nourished, he did not appear seriously ill. Results of the physical examination were normal, with the exception of the condition of the abdomen. There was moderate tenderness just to the right of the umbilicus, but no definite rigidity and no distention, the left lower quadrant was flat to percussion. The blood pressure was 128 systolic and 78 diastolic, temperature, 98.8 F, pulse rate, 90, respiratory rate, 20. The urine was normal, the leukocyte count, 15,600.

Exploratory celiotomy through a right paramedian incision was performed at 10 a m, on May 22, with the patient under ether anesthesia. The peritoneal cavity contained about 200 cc of free serous fluid, most abundant in the right upper quadrant. A portion of the small intestine, at the level of the junction of jejunum and ileum presented, for about 10 inches (25.4 cm) it was dilated, red and con-

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Submitted for publication, Jan 25, 1930

1 Demel, Rudolf. Ueber die Anzeigestellung zum operativen Eingriff bei stumpfen Bauchverletzungen, Arch f klin Chir **135** 542 1925

gested, with its peritoneal surface slightly glazed. It had the appearance of a loop of intestine strangulated for a short time in a hernial sac. Search of the entire abdomen revealed nothing further. The circulation of the portion of intestine involved appeared intact and the intestine viable. It was therefore replaced and the abdomen closed without drainage. The cause of the intestinal pathologic process was obscure and no diagnosis was made.

*Postoperative Course*—The temperature rose to 101.1° on the second day, but promptly returned to normal and remained so. The pulse rate never exceeded 100 and stayed around 80 most of the time. An enema secured good results. Three days after food was again given to the patient he vomited. The abdomen became markedly distended and tympanic relief being obtained by enemas. He began to pass large fluid stools frequently, six the fifth day and the sixth six the seventh and five the eighth day. There was no gross blood. He was given a liquid diet from the third to the sixth day and a soft diet after that. On the ninth day he complained of pain in the abdomen, not localized, and of severe pain in the lumbar region. The abdomen became markedly distended and tympanic but there was no vomiting. The patient was relieved by the use of morphine. He had a good night's rest and the next morning the distention had disappeared. There was a good bowel movement and he felt quite well. The next day he was out of bed in a wheel chair and had no further complaint. He had two or three large formed stools a day, and was discharged apparently in good condition fifteen days after the onset of his illness. At no time following his operation did he show any particular abdominal tenderness.

Nothing further was heard concerning him for two days when he was readmitted to the hospital on June 6 at 2 p. m. He stated that he had scarcely left after eating his noon meal, when he began to have abdominal pain. On arrival at home the pain became exceedingly severe and he vomited. He called his physician twice during the night in order to receive morphine. Pain and vomiting continued all the next day, and there was no bowel movement. Cathartics and enemas were taken without avail. He steadily became worse, and returned to the hospital. He was in a state of collapse with profuse sweating. The temperature was 97.2° F., pulse rate, 106, respiratory rate, 36. His abdomen was markedly distended and tense, though he complained little of tenderness on pressure. He was clear mentally. His temperature rapidly rose to 101° F., then to 102° F., the pulse rate rose to 140 and the respiratory rate to 50. He vomited fecal matter, and died at 4 a. m. on June 7, seventeen days after becoming ill.

At the time of his second entrance to the hospital, the following additional history was obtained. During the morning previous to the onset of his illness, while plowing, his plow-share struck a large rock and was thrown out of the furrow, and he was struck a brisk blow in the abdomen by the handle. He felt a little faint, but soon recovered and paid no further attention to it. He never mentioned the occurrence to either his family or his physician, thinking it insignificant and of no relationship to his illness. Also, just previous to leaving the hospital on June 4, he had gorged himself on a large amount of fresh strawberries which were smuggled into the institution by a relative.

At necropsy, gas escaped when the peritoneum was incised. The entire upper part of the abdomen from the level of the umbilicus to the area over the right lobe of the liver contained fecal material. The intestines of the upper and mid-portions of the abdomen were plastered together, the loops distended. The right flank was closed off by plastic adhesions, serous fluid being encountered when these were broken up. A large amount of dirty appearing exudate was in the pelvis. In

the lower jejunum in the midline just below the stomach and the transverse colon were two perforations on the antimesenteric border not over an inch apart, from which fecal material exuded

Examination of the involved portion of the intestine after removal (fig 1 and 2) showed on the peritoneal side the serous coat covered with plastic exudate, containing two cleancut, punched-out, more or less circular perforations, a smaller lower and a larger upper one. The surrounding tissue of the smaller one showed little change, that of the larger, a bluish-black discoloration extending almost



Fig 1 (case 1) —Peritoneal surface of specimen

one-half inch about the perforation, especially at the lower border, at the upper border, the omentum was plastered to the intestine up to the perforation but not covering it. On the mucosal surface, however, the involvement was much more marked and extensive. The lower smaller perforation was the same size as on the peritoneal surface. Just above it was a much larger denuded area, a shallow ulcer (partially covered in fig 2 by one of the valvulae conniventes) with a granulating base as if the mucosa had sloughed and the area was in process of healing. The perforation in the mucosa at the upper site of the involvement was larger than and not exactly opposite the hole in the peritoneum. To either side of it were two other smaller perforations while above it separated by a valvula



convexity, was a row of three other smaller mucosal perforations. The jejunal mucosa was thus completely undermined and separated from the other intestinal coats in the whole area of the six perforations.

CASE 2—A boy, aged 10 years, was admitted to the hospital on May 30, 1926. An hour and a half before, while playing, he fell off a box car and was struck across the upper portion of the abdomen. He said that he struck a rail; an observer said that he struck a bumper on the car. He complained immediately of severe abdominal pain and tenderness. However, he felt very much better on admission.



Fig. 2 (case 1)—Mucosal surface of specimen

though he vomited shortly thereafter. He lay on his right side with legs flexed. His temperature was 98 F, pulse rate, 100, respiratory rate, 36, blood pressure, 92 systolic and 60 diastolic. His general condition appeared good. His abdomen, however, was rigid all over, slightly more on the right, where there was also dulness to percussion. It was decided to observe him for an hour or two. His condition rapidly improved, and operation was not performed. Early the next morning, however, his temperature was 101 F, pulse rate, 100, and respiratory rate, 40. Vomiting recurred. By midafternoon, his condition was alarming. The temperature was normal, pulse rate, 140, respiratory rate, 40, blood pressure, 72 systolic and 65 diastolic. He appeared very ill, and was irrational. The left side

of the abdomen was now quite lax, the right, however, was rigid and slightly distended with a tender mass in the right upper quadrant and epigastrium. The next morning the boy was better, and by June 2, four days after injury, the storm had completely subsided, and he began to take nourishment. He had spontaneous stools from the second day on with no diarrhea. He was discharged on June 6, with no complaints and apparently in good condition.

On June 12 at 10 a. m., he again was seen in consultation. He had felt reasonably well for three days after discharge, and was up and about and out of the house playing. His mother had permitted him to be very indiscreet in his diet, he had eaten of everything and in very large amounts. On June 10, he had severe abdominal pain with marked distention and some vomiting. His physician gave him morphine, enemata, and applied hot fomentations, and he improved. However, severe pain in the region of the navel, abdominal distention and vomiting soon recurred. On examination, his abdomen was found markedly distended and tense with muscular rigidity and acute tenderness just to the right of the navel. His temperature was 100 F, pulse rate, 110 and respiratory rate, 24. He was at once returned to the hospital, but his condition rapidly became so critical that the idea of operative intervention was abandoned. About 5 p. m., he complained of severe abdominal pain, his pulse became very rapid and weak, respirations increased, cyanosis and cold sweat appeared, he had an involuntary fluid stool, and vomited a large amount of brown fluid. The whole abdomen was tensely rigid and flat on percussion. Death occurred at 6:30 p. m. on June 12, thirteen days after injury. Necropsy was not permitted.

#### REPORT OF CASES FROM THE LITERATURE

CASE 3 (Targett<sup>2</sup>)—A man, aged 40, was crushed between a rail of a barge and a crane. He vomited immediately after the accident. On December 1 at 8 a. m., he was admitted to the hospital in a state of collapse. There was considerable tenderness in the lower iliac region and a hematoma in the abdominal wall. He vomited frequently. There was no hematuria. The temperature was 101 F. Opium pills were administered ("Pil opii gr j 6 t'is horis"). On December 2, vomiting continued, the vomitus consisting of brownish material. There was no blood. The abdomen was tender on palpation, but there were no signs of distress. The patient was not at all under the influence of opium. On December 3, the patient was better. Respiration was quiet, and the temperature was normal. There was no pain, and less tenderness. The next day the patient was better and cheerful. He had had no sickness for thirty-six hours. He passed flatus freely. The temperature was normal. At 10 p. m., vomiting came on suddenly. No special pain was complained of, but sickness continued through the night. On December 5, persistent vomiting of brownish material with a fecal (') odor continued. The patient was very weak and faint. Cold perspiration was noted. The temperature was 98.4 F. On December 6, he was in a state of severe collapse. The pulse was imperceptible. There was occasional sickness. The vomitus was bright yellow. There was a bowel movement. The temperature was 97.6 F. At 8 p. m., when death occurred the temperature was 99.4 F.

Autopsy showed acute suppurative peritonitis with a large quantity of bright yellow fecal material in the abdominal cavity, and gas. There was a rupture in the small intestine 7½ feet (230.5 cm.) from the cecum, the bowel being glued

<sup>2</sup> Targett, J. H. Perforation of Intestine Four Days After Accident. *Tr Path Soc London* 38 143, 1887.

to the spine on the left side of the fourth lumbar vertebra. Scybala were found in the cecum and ascending colon. There was no fracture or injury to the other viscera.

CASE 4 (Brewer<sup>3</sup>)—A man aged 38 was struck in the midportion of the abdomen by a falling bale of paper. He experienced considerable pain at first but soon recovered. After his admission to the hospital he presented no evidence of shock. The pulse rate varied between 60 to 70 and was of good quality. Slight tenderness was elicited over the epigastric and hypogastric regions and an appreciable degree of muscular rigidity. No vomiting occurred. There were no signs of free fluid or gas in the peritoneal cavity. A diagnosis of visceral injury was made and an immediate operation advised. This was indignantly refused and the patient insisted that he felt perfectly well and was suffering only from a slight bruise of the abdominal wall. During the following night the pain increased, and the patient became restless and feverish. The next morning he appeared seriously ill. The abdomen was distended and tympanic; the liver dullness was not entirely obscured. Tenderness and rigidity were everywhere present. There was flatness in both flanks, which disappeared on changing the position of the patient. The white blood cells numbered 16,000.

Although it was recognized that the outlook was then well nigh hopeless, at the patient's request the abdomen was opened, ether anesthesia being used. As soon as the peritoneal cavity was opened a large amount of gas and foul-smelling cloudy fluid escaped, which was found to be a mixture of scopus and intestinal contents. The intestines in the lower half of the abdomen and pelvis were injected and covered by a fibrinous exudate. A large perforation was found in the lower third of the ileum, through which gas and fecal matter were constantly escaping. Several other severely bruised and ecchymotic areas were found on various coils of the small intestine. The rupture was united with two rows of Lembert sutures. The peritoneal cavity was thoroughly irrigated and the wound closed with two cigaret drains, one leading to the pelvis and one to the right flank. The patient received injections and he was generously stimulated. He did exceedingly well for more than a week. The temperature and pulse rate fell to normal; distention and rigidity disappeared; bowel movements occurred and the patient took plenty of fluid food. About the tenth day, he began to complain of pain and signs of a rapidly spreading peritonitis began to develop. Death occurred two or three days later.

Autopsy showed the original perforation to be healed, but a second perforation had occurred at the site of one of the contused areas seen at the time of operation.

CASE 5 (Eve, quoted by Deaver<sup>4</sup>)—A brakeman was injured by falling between the engine and car, his body being caught between the bumpers. He was unconscious for several hours. When Dr. Eve saw him first, he was still suffering from shock, and complained of great pain in the abdomen and back. He had several vomiting spells, the vomitus being dark and of an unpleasant odor, vomiting commencing three hours after injury. Examination of the back and abdomen brought on attacks of nausea, followed by vomiting of dark, offensive, stercoraceous matter. Examination of the back after the patient became quiet,

3 Brewer, George Emerson. Contusions of the Abdomen Associated with Visceral Injury, *Illinois M. J.* 48:70, 1925.

4 Deaver, John B. The Symptoms, the Diagnosis and the Indications for Treatment of Acute Intra-Abdominal Injuries Without External Evidence of Violence, *Railway Surg.* 3:97, 1896-1897.

revealed two large excoriations extending from the ninth dorsal vertebra to the sacrum. There were no excoriations or evidence of internal injury on the abdomen, although it was tympanitic and tender. He had had no action of the bowels for five or six days prior to the injury. The temperature was 101 F, the pulse rate 130, respiration 28. Free evacuation of the bowels was followed by decrease in the pain; the pulse became stronger; the temperature fell to 100 F, and the abdomen became flaccid. Examination of the abdomen at this time gave negative results. The patient slowly improved and by the end of the fifth week was able to get out of bed and to walk about the room. About the sixth week he complained of some colicky pain in the abdomen, which was attributed to fermentation of food. About the ninth week he suddenly had severe pain in the bowels, accompanied by an audible gurgling sound and a knotting of the intestines, which could be plainly felt through the abdominal walls. Some weeks later a tumescence developed in the hypogastric region, extending to the left inguinal region and reaching as far back as the lumbar region. There was no fluctuation. On the following day, an abscess broke, and a large quantity of pus accompanied by gas of a decidedly fecal odor was discharged. The following day fecal matter escaped through the opening. An operation for relief from the fistula was performed but the patient rapidly sank and died shortly afterward.

CASE 6 (Bunge<sup>5</sup>) — A man, aged 49, had been well except that for several years he had had inguinal hernias which were easily kept reduced and held in place by a truss. While lifting a heavy mass to put it on his shoulder he felt a severe pain in the abdomen, which he localized to the right, but he was not sure. The pain soon subsided sufficiently for him to continue working and during the next thirty-six hours, as was confirmed by his relatives, he felt quite well. Urination and defecation were normal. In the night renewed pain appeared, associated with vomiting. Vomiting became more severe, first of blood (?) and at last of fecal matter. About fifty-four hours after the first attack of pain he was received at the clinic. He was poorly nourished, with a small but regular pulse (from 100 to 110). The abdomen was not particularly distended, but was quite tender throughout; the abdominal walls were hard as a board. Both inguinal rings admitted the index finger, but no sac was felt on either side. Palpation of the rings, especially the right, elicited marked tenderness. There was dullness to percussion on the left, less on the right. On the left could be seen a markedly distended intestinal loop. By rectum, one felt a sense of resistance in the culdesac; pressure was very painful. Operation was performed immediately. An incision was made in the midline from the navel downward. Foul-smelling exudate immediately welled upward. The intestines were partially plastered together by fibrinous purulent exudate. Palpation of the inguinal rings from the abdomen showed that both admitted the tip of the index finger. There were no definite hernial sacs but merely slight outpouchings of the peritoneum. Near the right internal ring was a coil of small intestine which contained an opening about the size of a pea. Surrounding the perforation, the intestine was colored bluish red as if infarcted. The borders of the perforation were fairly smooth and granulating, and the mucous membrane was not prolapsed. There existed, therefore, a defect which appeared as if it had arisen from the sloughing of a necrotic area. The perforation lay about 1.25 meters from the ileocecal junction opposite the mesenteric attachment. It was closed by a two layer running stitch; the abdominal cavity was washed out with physiologic solution of sodium chloride and gauze drainage was inserted.

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<sup>5</sup> Bunge. Zur Pathogenese der subkutanen Darmrupturen. Beitr. z. klin. Chir. 47: 771, 1905.

Death occurred ten hours later. At necropsy, besides the diffuse peritonitis, there was an encapsulated subphrenic abscess on the right. The intestinal suture was intact.

#### COMMENT

The foregoing case reports from the literature have been added to my own cases because they illustrate certain variations in the picture of secondary intestinal perforation, that of Targett represents an early perforation four days after injury, that of Brewer, perforation of a contused area after recovery from a primary perforation closed at operation, that of Eve, very late perforation weeks after injury, with formation of abscess and fistula, that of Bunge, perforation from indirect trauma.

Secondary or late perforation of the small intestine from trauma is rare. Demel<sup>6</sup> reported no instance in his study of 126 cases of abdominal injury, and similarly, Hagen<sup>7</sup> none in his 104 cases. Morton,<sup>8</sup> in his tables of 234 cases of abdominal section for trauma, cited only 1 that I can place in this group.<sup>9</sup> It would seem therefore, that this complication plays but a minor role, and that in comparison with either primary intestinal perforation or mild intestinal contusion without perforation it is infrequent.

*Pathogenesis*.—Injury to the abdomen may be local or general. Damage to the intestine from such trauma has generally been divided into three forms: (1) contusion or crushing (ecchymement, Zerquetschung), (2) tearing (dehincence, arrachement, Abriss durch Zug) and (3) bursting from increased pressure within the intestinal lumen (eclatement, Berstungsrupture). I discussed this general problem of intestinal injury in a previous publication.<sup>1</sup> In this paper only contusion or crushing is considered, and indeed, only crushing of such limited severity that primary perforation of the intestine does not occur. Likewise, I am chiefly concerned with local trauma in contradistinction to general, for the latter is often apt to be much more severe, and in these severer injuries other organs are generally included, frequently with profuse hemorrhage and shock, so that intestinal contusion if it occurs is only a small part of the clinical and pathologic picture. In local trauma, however, injury may be easily limited to the midportion of the abdomen. In the cases here reported, it resulted either from a direct blow, or from catching of the body between two

6 Hagen, W. Ueber Bauchverletzungen des Friedens, Beitr. z. klin. Chir. **51** 529, 1906.

7 Morton, Thomas S. K. Abdominal Section for Traumatism with Tables of Two Hundred and Thirty-Four Cases. J. A. M. A. **14** 1 (Jan. 4) 1890.

8 Bouilly. Bull. et mem. Soc. de chir., 1883, p. 690.

9 Inlow, W. D. Abdominal Trauma with Intestinal Injury, J. Indiana M. A. **38** 237 (June 15) 1929.

objects with compression and crushing. Besides types of direct injury, Bunge<sup>9</sup> has shown that a like result can occur from indirect injury. Bunge, in the discussion of his case (case 6), called attention to the fact that there was a definite intermediate stage in which symptoms of a well defined peritonitis were absent following the injury. He therefore reasoned that one of two things happened. There might have occurred a small primary tear of the intestine, which was walled off by adhesions, and a generalized peritonitis occurred secondarily. He considered this explanation improbable. On the intestine which was pressed into the inguinal ring at the moment of the increase in intra-abdominal pressure was severely injured, but not brought to rupture, and perforation occurred later. In support of this view, he cited both the clinical course and the involvement in the intestine. The perforation definitely appeared as if it had taken place through the sloughing of a sequestered piece of intestinal wall. If the latter explanation is correct, his case is rightfully one of late perforation, and affords the only example I have been able to find in which such perforation was the result of indirect and not direct trauma.

To produce a contusion or crushing of the intestine, a firm object must push in the abdominal wall with compression of the intestine against a rigid background. Since the locations of such contusions have been found directly over the spinal column, it may be deduced that the latter structure generally furnishes this required background. The intestine is so damaged that perforation occurs either immediately or after a variable length of time owing to secondary gangrene of the wall, thus late perforation generally happens about two weeks after the initial injury. However, in Targett's case perforation occurred in four days and in Eve's, in three months.

Naturally, the severity of the force has much to do with whether the intestine is ruptured immediately or merely contused. Likewise, the tenseness or tautness of the abdominal muscles at the time of impact is important. Generally, the recipient of an abdominal injury is caught by surprise, and the abdomen is lax. Occasionally, however, sufficient time is given for the victim to contract his abdominal muscles and partially dissipate the violence of the blow. It is true also, that a reflex contraction of the abdominal muscles occurs at the moment the object strikes the abdominal wall, but quite often this comes too late to diminish the force of the blow.

In contusion of the intestine, according to Hertle,<sup>10</sup> it is the mucosa that is injured first, while the other layers remain intact. The mucous membrane is crushed over a greater or less extent, the edges of the

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<sup>10</sup> Hertle, Josef. Ueber stumpfe Verletzungen des Darmes und des Mesenteriums, Beitr. z. klin. Chir. 53: 257, 1907.

wound are often irregularly star-shaped, and the mucous membrane for a distance surrounding is separated from its underlying layers. This separation is well demonstrated in the specimen from my first case. If the crushing injury is more marked, the other intestinal layers are also involved, the peritoneum being generally quite resistant and showing relatively slight defects.

Eichel<sup>11</sup> has studied the effects of localized abdominal trauma in dogs. With the animals anesthetized even severe blows were innocuous when the test were tied down tight regardless of whether the intestinal tract was full or empty. Apparently the stretching of the abdominal muscles made the strongest blow harmless. Only when the hind legs were loosened and the abdomen made lax and blows were delivered in the midline over the spinal column were intestinal and mesenteric lesions secured. Blows in the lumbar region with legs flexed even during full digestion and after filling the rectum with air, had no effects. However, blows struck dogs that had been operated on and as a result had adhesions to the abdominal wall or between the intestinal coils caused severe injuries.

Von Angerer,<sup>12</sup> in discussing intestinal contusions remarked that they are recognizable by suffillation and ecchymosis in the intestinal wall and the bluish color of the serosa. Surgeons have the opportunity to see such contusions when forced efforts at taxis have been made in incarcerated hernias. The degree of severity of such contusions is difficult to judge, but he stated that one is accustomed in general to attach no undue importance to them when the serosa is intact. However, if tears can be recognized in the mucosa and in the muscularis, the danger of a later perforation is very great. The first case here reported would seem to belie this statement. The serosa was intact at the time of the exploration and the intestine seemed viable, but perforation occurred nevertheless. However, there is probably another factor besides that of mere contusion or crushing of the intestine that contributes materially to the necrosis of the intestinal wall and ultimate perforation. This contributory factor is distention.

When a portion of the intestine is contused, the area involved is so crippled and parietic that when it is called on to do work, as when the patient is fed, it is unable to contract properly and acts as a point of obstruction. Following this, the intestine above the lesion becomes markedly distended, as may readily be seen in the clinical histories here given. I quote from Van Beuren:<sup>13</sup>

11 Eichel. Klinischer und experimenteller Beitrag zur Lehre von den subkutanen Darm- und Mesenterium-Verletzungen, Beitr z klin Chir **22** 219, 1898.

12 Von Angerer. Ueber subcutane Darmrupturen und ihre operative Behandlung, Arch f klin Chir **61** 970, 1900.

13 Van Beuren, Frederick T., Jr. The Mechanism of Intestinal Perforation Due to Distention, Ann Surg **83** 69, 1926.

Distention of the intestine increases its diameter. Any increase in its diameter is tripled in its circumferential measurement. A moderate increase in diameter, therefore, results in considerable stretching of the wall. The intestinal vessels pass between the layers of the wall along its circumference from their origin at the mesenteric border to their terminal anastomoses at the antimesenteric surface, becoming progressively more thin-walled and more narrow of lumen. Because they are elastic the stretching of the intestinal wall from distention still further thins the vessel walls and narrows the vessel's lumen like a stretched rubber tube. At the same time the pressure from within the intestine tends to flatten out the vessel's lumen. The narrowing of the vessel's lumen and the thinning of the vascular wall are maximum at the antimesenteric surface of the intestine where the terminal anastomoses occur, and, the distention pressure being constant throughout the lumen of the intestine, the maximum effect is seen at the antimesenteric surface where a union of the three factors of pressure, thin wall and narrow lumen finally results in obliteration of the vessel. This obliteration occurs sooner in the vein than in the artery on account of the less resistant wall. The blood continues to pour through the arterial vessel until the pressure against the obliterated vein suffices to rupture the vessel wall and permit extravasation and coagulation. Finally, the pressure occludes the artery as well as the vein. The area of tissue supplied by these terminal vessels is thus deprived of circulating blood and necrosis occurs. This necrosis is usually first evident in the submucosa and inner muscular coat, but rapidly extends to the other coats of the intestinal wall, and perforation may occur within twenty-four hours after the discoloration due to the hemorrhagic infarct has been first noticed.

Further, the question may be asked, what rôle if any do the intestinal digestive juices play in the causation of perforation? I have no definite data on this point. Doubtless, in the lower ileum this factor can be disregarded, and it is in this location that most of these perforations occur (in four of six cases here reported). But in the jejunum, the question may deserve more consideration. Case 1 comes under this category. As seen in figure 2, the healing ulcer on the mucosa below the areas of perforation looks not unlike a shallow peptic ulcer, and the thought naturally arises that tryptic activity may have had some part in its causation. In this connection, a case reported by von Huebschmann<sup>14</sup> is of interest. A boy, aged 4½ years, suffered a slight abdominal trauma four weeks before death. Following the injury he had persistent intestinal bleeding, and finally peritonitis with a fatal outcome. At necropsy, a perforation of a Meckel's diverticulum, which was entirely coated with gastric mucosa, was found. Presumably a tear in the mucous membrane caused by the trauma was converted into an ulcer through peptic action which later led to perforation. This, of course, is a case illustrating the now comparatively well

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<sup>14</sup> Von Huebschmann. *Munchen med Wchnschr*, September, 1913 pp 2051-2052, quoted by Stulz and Voringen. *Peptic Ulcer of Meckel's Diverticulum* *Ann Surg* **83** 470, 1926



known picture of peptic ulcer of this diverticulum, but it is of interest that peptic activity, and not distention, added to the trauma played the decisive rôle in leading to perforation.

*Clinical Course*—There are no distinctive symptoms of intestinal injury. Trauma to the abdomen varies in severity from mere slight contusion of the parietes through various degrees of intestinal contusion to severe ruptures of the intestinal tract, and often it is difficult to know how extensive the damage is. Furthermore, the picture may be obscured by injuries to other organs with hemorrhage. Yet on the whole, those cases in which only intestinal contusion occurs show a less severe degree of trauma and a less striking clinical course than those in which primary perforation takes place. Yet at times the gravest lesions may exist with few symptoms. Indeed, abdominal trauma in its initial phase should be considered as a whole, and contusion and primary perforation separated only at the operating table. The clinical course may conveniently be divided into three stages: an initial, an intermediate and a terminal.

In the initial stage, the patient enters the hospital with the history of having suffered abdominal trauma of varying severity. This history, however, may be entirely lacking as in case 1, in which the blow received seemed so trivial to the patient that he did not even mention it. Pain, often severe, diffuse or located in the midportion of the abdomen, is the most constant symptom. Vomiting may occur. There are generally no external evidences of injury to the abdominal wall. Among the foregoing cases only one showed excoriations, and these were on the back. Abdominal tenderness is invariable, and together with the pain, constitutes the most reliable sign. It may be diffuse or localized to the area of injury. Rigidity and distention may or may not be present. Heineke<sup>15</sup> has discussed marked meteorism coming immediately after abdominal trauma. This he attributed to injury to the retroperitoneal nerve plexuses. It generally occurs in mild injuries and is absent in severe visceral lesions until the onset of peritonitis. Generally the temperature is at first normal, though the pulse and respiratory rate may be accelerated. Soon, however, the temperature rises, but seldom above 101 F. The symptoms may become alarming, as for example in case 2, and if expectancy has been practiced, one judges he has erred in not opening the abdomen, that a perforation has been present, and that fatal peritonitis is developing. Yet this storm may subside almost as rapidly as it came.

The intermediate stage is one of relative quiescence. The danger seems to have been safely passed, and all concern is lost with conse-

15 Heineke, H. Ueber Meteorismus nach Bauchcontusionen, Arch f klin Chir 83 1104, 1907.

quent relaxing of the previous careful observation. The patient may be dismissed from the hospital and forgotten, only to be later readmitted in an agonal state. Yet tokens of the impending catastrophe are presented if they are only read correctly. With the least dietary indiscretion, pain recurs. Intermittent distention persists past the time at which it seems it should have completely disappeared. Diarrhea may occur and blood may be found in the stool. This intermediate stage is of variable duration, generally lasting from ten days to two weeks, exceptionally, from four days (case 3) to three months (case 5).

In the terminal stage, perforation occurs. Pain is very severe, it is that of perforated peptic ulcer. This is in marked contrast to the pain of primary intestinal perforation, when the patient may insist that there is nothing wrong and refuse operation. Following perforation, the symptoms are those of a fulminating and rapidly fatal peritonitis. Vomiting recurs and soon becomes fecal. The abdomen is distended and rigid, and may be flat to percussion. The pulse rate rises. The blood pressure falls. Cold sweat and cyanosis appear. There may be involuntary stools. Death swiftly follows. The loss is dramatic, coming as it does after apparent recovery from the initial injury. After perforation, the hopelessness of the situation is only too evident and generally no intervention is attempted.

However, the course as depicted is not always followed. Perforation may not occur until after several weeks, and may be so slow that the area can be walled off by adhesions, and produce only a localized abscess or fecal fistula.

*Prognosis*—It is probable that mild contusions of the intestine are much more frequent than those progressing to secondary perforation. Many of these are not, and often cannot be diagnosed without exploratory laparotomy. Often patients with such injuries do not even consult a physician. At times, however, symptoms from intestinal contusion have been sufficient to lead surgeons to open the abdominal cavity, fearing that a serious visceral lesion existed. In such cases, exploration has given negative results with the exception of a bruise on the intestine, and prompt and satisfactory recovery has occurred on simply returning the intestine to the abdomen without further intervention. On the whole, then, the prognosis of intestinal contusion is favorable, most patients recovering without treatment. Hopp<sup>16</sup> reported four such cases of simple contusion in which operation was not performed and the patients were dismissed from the hospital in from six to fifteen days. Even in those cases in which symptoms do not promptly subside the outlook is probably fairly good if the danger is recognized.

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16 Hopp, Max. Ueber die Indikationsstellung bei traumatischen subkutanen Bauchverletzungen. Beitr. z. klin. Chir. 72: 278, 1911.

and the intestine is put at rest or operation performed. Blood in the stool is inconstant, but even when it is present it is not necessarily of bad prognostic import or necessarily indicative of impending perforation. It may indicate merely superficial mucosal ulceration which will readily heal. Hopp cited a case in point.

Yet when secondary perforation has occurred, the outlook seems hopeless. Death occurred in all the cases here reported, and a similar outcome has been reported in all other cases that I have found in the literature. Operation, even when done immediately, seems to be of little avail. In one of Hopp's three cases, operation was performed immediately with a fatal outcome. One would expect, however, that in some cases of very late perforation with abscess or fistula formation the outcome would be more happy than in Eve's case (case 5).

*Treatment*—As may readily be seen from the discussion on prognosis, the treatment for secondary intestinal perforation from trauma is prophylactic rather than curative. All effort must be directed toward the prevention of the catastrophe of perforation. The most important desideratum in this connection is the knowledge of the possibility of this contingency, the factors in its causation and the signs of its imminence. Had I been sufficiently conversant with this syndrome, the patients in the two cases here reported would not have been dismissed from the hospital, indiscretions in diet would have been avoided, and secondary intervention would have been resorted to before perforation. In extenuation it might be said that in the first case no history of injury was elicited, and every one was entirely at sea as to the nature of the underlying pathologic process. In the second case, no such excuse is possible, indeed, still further censure could be made in that exploratory celiotomy was not made at the time of injury.

I need not discuss in detail the treatment of the first stage, since it is that of abdominal injury in general. The patient should be hospitalized. Shock, if present, should be promptly combated. The abdomen should be immobilized by a binder. Morphine should be used sparingly, especially in cases in which exploration is not done immediately for thus the progress of the case may be unduly masked. If there are good grounds for suspicion of visceral injury (pain, rising pulse rate, tender and rigid abdomen, especially over a limited area), exploration should be made at once. At this intervention, primary intestinal rupture may be found or areas of contusion associated with such rupture or merely intestinal contusions alone. In the second of these, it is not sufficient to repair the rupture alone and disregard the areas of contusion. These accompanying contusions should receive the same careful attention that they would if they were the only lesions present. The peril inherent in these contusions is well shown in Brewer's case.

(case 4), in which, after successful repair of a primary intestinal perforation, a secondary perforation occurred ten days later at the site of a contused area seen at operation

It is the treatment of the second or intermediate stage of abdominal trauma that especially belongs to a discussion of secondary intestinal perforation. The prodromal symptoms of perforation (pain, vomiting, diarrhea, blood in the stool, localized tenderness, meteorism) should be carefully watched for, and on their first appearance, the intestinal tract should be put at rest. All foods should be promptly discontinued, and the patient given fluids by rectum or under the skin. Hertle<sup>10</sup> advised continuance of this fast for five days. If the symptoms promptly subside, careful resumption of diet should be made, starting with liquids. Marked distention, if present, should be relieved by enemas, since such distention is probably more dangerous than any peristalsis so set up. Narcotics should be used sparingly, especially during the observation period. If the threatening symptoms do not promptly subside, or if after subsidence they reappear on the least attempt at feeding, intervention would seem to be indicated, though I have found no case in the literature in which this has been carried out before perforation. At operation, the area, if small, may be turned in by suturing, or covered by omentum or sutured to some peritoneal surface (parietal peritoneum), if large, it should be resected.

This has been tried out by Thomson<sup>17</sup> in experiments on dogs in which portions of the wall of the intestine were excised. He has shown that small lesions not larger than 1 cm square can be safely sutured over, provided the surrounding tissue is normal. Larger defects, if resection cannot be carried out or is difficult, can be handled by a plastic operation with fixation of the intestine to an adjacent peritoneal surface so long as an acute knuckling is avoided. However, deep intestinal defects, even if of small extent where the surrounding wall is pathologic, should be treated by resection, if this is not possible, a plastic covering should be made and gauze drainage instituted. In my first case mere covering of the involved area of intestine at the time of operation might have converted the case from one of free peritonitis after perforation to a localized abscess which later could have been successfully drained. The effort made by the tip of the omentum to plug the upper perforation can be seen in figure 1. In cases of marked distention, ileostomy above the lesion should be considered.

Treatment at the third stage after perforation seems hopeless. Possibly immediate intervention with closure of the perforation and drainage may in the future show better results than in the past, for

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<sup>17</sup> Thomson Hermann. Ueber nicht perforierende peritonale und muskuläre Darmläsionen und deren Behandlung. *Ztschr f Geburtsh u Gynäk* 26 163 1893

this effort has only occasionally been made, and there are not enough available data to enable one to come to final conclusions

#### SUMMARY

1 Six cases of secondary or late perforation of the small intestine from trauma are reported, two personal, and four illustrative ones from the literature. On the basis of these reports, a clinical discussion of the condition is given.

2 Secondary perforation results from the necrosis and sloughing of an area of the intestinal wall, on the antimesenteric border, which has been contused, generally either from direct blows over the mid-portion of the abdomen or from crushing. Intestinal distention is a contributing factor. Perforation occurs most frequently about two weeks after injury.

3 The initial symptoms are those of abdominal trauma in general. After apparent recovery, there are symptoms in the intermediate stage suggesting the possibility of late perforation, these are recurring pain and tenderness, vomiting, meteorism, diarrhea and blood in the stool. The pain of perforation is similar to that of perforated peptic ulcer. A fulminating and rapidly fatal peritonitis ensues.

4 The prognosis of simple intestinal contusion is good. Most such contusions heal without being diagnosed. When necrosis with secondary perforation occurs, however, the outlook is bad, all the cases here reported having proved fatal.

5 The initial treatment is that of abdominal trauma in general. If visceral injury is suspected, exploration should be performed at once. Areas of contusion should be protected by being turned in if very small or covered by omentum or sutured to the parietal peritoneum if larger. Primary resection is required only occasionally. In the intermediate stage perforation may be guarded against by a careful dietary regimen, with periods of absolute withdrawal of food if necessary. Patients should be kept in the hospital until all danger is past.

# THE PROBLEM OF CANCER OF THE STOMACH\*

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AND

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DETROIT

That cancer of the stomach is a problem, and can be considered a major problem in the control of cancer, is evident when one considers the figures of the annual toll of cancer in this part of the body, how little actually is accomplished for the patient with cancer of the stomach and what might possibly be done for him

The general facts are well known Almost 35 per cent of all deaths from cancer are due to cancer of the stomach the disease picture is easily recognized when well developed, large series of successful primary removals have been reported, yet the general hopelessness and pessimism of most laymen and physicians are only too apparent

This study is based on an analysis of 365 consecutive deaths from cancer of the stomach, collected through the Cancer Division of the Department of Health Of these patients, 213 were observed in hospitals and 152 were not<sup>1</sup> The points borne in mind were (1) the present average situation as regards diagnosis and treatment, (2) the chief difficulties and commonest errors in both recognition and therapy and (3) the possibilities for improvement and control

## THE AVERAGE CARE

It is easily seen that, viewing the average situation as regards diagnosis and treatment, the popular pessimism concerning cancer of the stomach is well founded (table 1) In other words just 3 per cent of those who died had had the chance of cure which operative recovery from radical resection represents The series covered one and a half years and included all deaths registered as having been caused by cancer of the stomach in a population of 1,730 000 during that time As indicated in previous studies, this can probably be considered an average situation, it is believed that similar tabulations in most of the com-

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\* Submitted for publication Jan 7, 1930

1 All deaths were certified as having been due to cancer of the stomach In many instances, the diagnosis was made clinically only, so that a certain amount of scientific accuracy may be lacking in these analyses however a death with dyspepsia, vomiting loss of weight epigastric mass etc was considered certain enough to have been caused by cancer to be included for analysis Unless the cases which had had only clinical observation showed these manifestations, they were not included

munities the country over would show similar figures, so that, as regards the average possibilities of accomplishment, the start can be made almost at the level of zero

#### THE CHIEF DIFFICULTIES AND COMMONEST ERRORS IN RECOGNITION OF CANCER

Though some well qualified internists still insist that cancer of the stomach cannot be recognized by present diagnostic methods early enough for any accomplishment in radical treatment, nevertheless authors of textbooks are rewriting the text on symptomatology of this type of cancer,<sup>2</sup> leaving out the description of the terminal condition—mass, vomiting, loss of weight, pain, etc—and describing the early mild manifestations. It is well recognized that one of the chief factors in any possible improvement in the treatment of cancer of the stomach will be earlier recognition.

TABLE 1—*Care Given in a Series of Fatal Cases of Cancer of the Stomach*

Total number of deaths from gastric cancer	365
Total number in hospitals	213
Total number of operations	96
Exploration only	29
Gastro-enterostomy	35
Gastrostomy, etc	4
Resections	28
Total primary recoveries from radical operations	11 or 3%

Three hundred of these 365 charts were analyzed. The first symptoms given in the 300 histories were studied. The histories of patients with cancer of the stomach can easily be divided into those which indicate a previous indigestion of several years' duration of more or less severity and those in which the cancer started suddenly from apparently good health. Of 287 cases in which such data were obtained, 71, or 24.7 per cent, started from long preceding indigestion. The remaining 216, or 75.3 per cent, started suddenly from previous good health. This shows a somewhat larger number starting from preceding indigestion than a previous analysis<sup>3</sup> (based on fewer cases) showed, and it is slightly higher than the number given in many reports. However, any large series of cases of cancer of the stomach will show 15 per cent or more starting from long continued preceding indigestion.

We shall consider first the larger group, the 75 per cent which started from previous good health. Table 2 lists the first symptoms complained of, in the order of their frequency, and divided further

2 Tice. Practice of Medicine, Hagerstown, Md, W. F. Prior Company, 1922, vol. 7, p. 496.

3 Saltzstein, H. C., and Sandweiss, D. J. The Average Treatment of Cancer, Arch Surg 18:2176 (April) 1929.

into those referable to the upper part of the alimentary tract—indigestion, history of ulcer, etc., presumably easier to recognize—and those not so definitely referable to the stomach and more atypical, as loss of weight, weakness, etc.<sup>4</sup>

Thus, 69 per cent started with symptoms which, though often mild, were distinctly referable to a pathologic disturbance in the upper part of the abdomen. The chief problem is not the recognition of the symptoms, but the arousal of suspicion that they may be of serious import. As McCarty expressed it<sup>5</sup> "Small cancers of the stomach

TABLE 2—*First Symptoms Complained of by Two Hundred Thirteen Persons Who Died of Cancer of the Stomach (Onset from Previous Good Health)*

Symptoms Referable to Upper Part of Alimentary Tract		Atypical Symptoms	
Indigestion	74	Loss of weight weakness	37
Pain in epigastrium	21	Loss of appetite	14
History of ulcer	20	Atypical pain (not in upper part of abdomen)	11
Vomiting	15	Anemia	2
Gastric hemorrhage	3	Diarrhea	2
Difficulty in swallowing	5		
Gnawing sensation in epigastrium	3	Total	66 or 31%
Distended abdomen	3		
Fulness in stomach	3		
Total	147 or 69%		

TABLE 3—*Contrasting Symptoms of Onset of Pyloric Cancer with Symptoms of Growths Starting Elsewhere in Stomach*

Cases	Location	Onset with Dyspepsia %	Onset with Atypical Symptoms %
55	Pylorus	70.3	29.7
36 *	Elsewhere	33.3	66.7

\* Lesser curvature 13, cardia 5, pars media 4, greater curvature 3, lesser and greater curvature 3, lesser curvature and cardia 3, fundus 2, total 36.

do not give signs and symptoms differing from those of chronic gastric ulcer, duodenal ulcer and sometimes disease of the gallbladder.

The number of cancers of the stomach that start suddenly with vague and atypical symptoms has given rise to a good deal of pessimism regarding the possibility of diagnosis early enough for radical treatment. When one considers this in the light of the anatomic location, the popular pessimism must be diluted.

In 91 of these cases with suddenly appearing indigestion the anatomic lesion was known with certainty.<sup>4</sup> Table 3 shows that 29.7 per cent of the pyloric cases started with atypical symptoms, contrasted

4 Data were incomplete in three cases, leaving 213 for analysis.

5 McCarty, W. C. *Cancer Research* 12:1 (March) 1928.

6 Cases in which the anatomic site of the lesion was not clearly stated as "pylorus and greater curvature," etc., or in which the site was not known with certainty were excluded.



with 66.7 per cent of those located elsewhere (lesser curvature, fundus, cardiac, etc.) starting atypically. As is shown in table 9, most of the growths resection of which was attempted were in the pylorus and distal portion of the stomach, so that as regards possibility of control, the pylorus and right half of the stomach is the important part.

That pyloric growths are twice as apt to start with typical symptoms as those elsewhere in the stomach, and that numerically more of the cancers that start with insidious unrecognizable symptoms are in non-resectable locations can only be facts of hopeful import when one is considering the control of cancer of the stomach.

*Danger of Confusing Ulcer and Cancer*—The argument as to whether ulcer precedes cancer of the stomach frequently enough to make medical treatment of gastric ulcer dangerous still waxes heatedly.

TABLE 4—*Symptoms of Onset of Cancer in Seventy-One Patients Who Had Had Long Continued Preceding Indigestion*

Onset of Cancer Symptoms Marked by	Preceding Symptoms Typical of Ulcer	Preceding Symptoms of "Dyspepsia"	Total
Recurrence of indigestion	9	6	15
Intensification of indigestion	7	32	39—76%
Weakness, loss of weight	2	5	7
Hemorrhage	1	1	2
Anorexia	0	1	1
Vomiting	1	3	4
Atypical pains	1	2	3—24%
	<u>21</u>	<u>50</u>	<u>71—100%</u>

Most pathologists, studying gastric cancers at autopsy or resected gastric ulcers, feel that the possibility of gastric ulcer developing into cancer is unusual, from 3 to 6 per cent being often quoted estimates. Surgeons have frequently estimated the possibility much higher, from 10 to 20 per cent or even more.

As noted, 71, or 24.7 per cent, of the total number of cases were preceded by a long continued indigestion, before symptoms of what was considered as the onset of cancer supervened. To be sure, there is no way of knowing whether these were gallbladder dyspepsias, slowly growing primary cancers, cancers developing on an irritable stomach or gastric ulcers that later developed into cancer. Since in most of these cases the preceding indigestion was of more than three years' duration and the average total duration of illness in all of the 287 cases was 15.6 months, it is not felt that many slowly growing primary cancers were included.

The symptoms of onset of 71 cancers that developed from preceding indigestion which may or may not have been due to ulcer are analyzed in table 4. In 76 per cent the only onset of what might have been the

change from ulcer to cancer was a recurrence of the symptoms after the lapse of a free interval or a sudden intensification of these symptoms. In 24 per cent, the probable onset of cancer was marked only by weakness and loss of weight, anorexia, hemorrhage, vomiting or atypical pain.

One third (21) of these cases of cancer with a long continued preceding indigestion were marked by typical postprandial pains relieved by alkalis and food. Over one half of these with the history of ulcer (14) had been clinically diagnosed ulcer, and presumably the patients had been treated for ulcer. Several of the patients had had medical management for ulcer within a few months of the positive diagnosis of cancer. Six had previous gastro-enterostomies (including 2 of the 14 who also had medical management for ulcer).

In addition to the cases just mentioned, 21, or 10 per cent, of the 216 cases that started suddenly from previous good health, had what was noted as "ulcer history." (This makes 15 per cent of the total 300 cases, which had "ulcer history" definite enough to be described as such.)

One cannot review these records without feeling that the practical problem of clinically confusing gastric ulcer with cancer is much more frequent than is represented by the estimate of 6 per cent. Generally, the cancer developed under the eyes of physicians other than those who treated the patient for ulcer and many of these cases would not come to the pathologist studying his hospital or autopsy material in regard to gastric ulcer and cancer, for in the second instance the cancer was well developed and its origin from possible ulcer obscured. Frequently, there being no second operation or autopsy, the diagnosis of cancer can be made only clinically and hence is always open to the criticism of the lack of scientific evidence.

The following cases are typical of the latent danger in conservative treatment for chronic gastric ulcer.

CASE S155—A woman, aged 61, had a gastro-enterostomy in January, 1922, for pyloric ulcer, following a history of peptic ulcer distress for thirty years. In January, 1925, three years after operation, there was a recurrence of abdominal pain, with vomiting, hematemesis, blood from the bowels and loss of weight. The patient refused operation for a suspected recurrence of the ulcer, and continued to lose weight, and to vomit. Had severe abdominal pain, developed a mass in the epigastrium and died in October, 1927, of what was clinically considered gastric carcinoma. There was no autopsy.

CASE S52—A man aged 53 had had indigestion—belching flatus etc—for twenty-six years for which gastro-enterostomy for pyloric ulcer was done in 1924. He felt perfectly well, was free from all pain and indigestion for one year after operation and gained from 109 to 145 pounds (49.4 to 65.8 Kg.) in weight. One year after operation cachexia began. There was a rapid loss of weight. Jaundice was marked during the last month of his life. He died in

May, 1927, two years after the onset of recurrence with what was clinically considered gastric carcinoma. There was no autopsy.

The chief problem is, just as it is with the lump in the breast, how often can one be sure that the lesion is benign without removing it?

Alvarez<sup>7</sup> analyzed some of the factors that tend to minimize in the minds of laity and physicians the frequent association of these two lesions. Gastric ulcer is relatively a rare disease. Large gastric ulcers are still rarer. Ninety-two per cent of the excised gastric ulcers are smaller than a 25 cent piece (2.4 cm). Also, 75 per cent of observed cancers of the stomach are larger than 4 cm, few are smaller than 2 cm. Practically, large gastric ulcers (over 2.4 cm) or small cancers (smaller than 2.4 cm) are so rare that a physician may not see one for several years, and hence is not often confronted with the clinical problem of differentiating gastric ulcer from cancer. But all cancers must be small at some time in their history. Alvarez estimated that on the basis of size alone a lesion in the stomach the size of a dime (1.8 cm) has one in fifteen chances of being malignant. If it is the size of a quarter (2.4 cm), there is one in ten chances of its being malignant. When it reaches the size of a half dollar (3 cm) there are two chances to one that it is cancer, and when it is larger than a dollar (3.5 cm) it is almost certainly cancer.<sup>8</sup>

*Roentgen Diagnosis*—Sixty per cent of these 300 cases were examined by means of the x-ray. In 30 per cent of the cases note was made that no x-ray picture had been taken. The data on the remaining 10 per cent do not indicate whether or not roentgenologic examination had been made.

As seen from table 5, 82.5 per cent of those who had been observed in hospitals had had roentgen examination, while only 26.1 per cent of those not in hospitals had had roentgen examination. The large number of patients with cancer of the stomach who die without ever having been in a hospital and without ever having had a roentgen examination or adequate diagnosis is perhaps not sufficiently appreciated. Many of

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7 Alvarez, W. C. Sizes of Resected Gastric Ulcers and Gastric Carcinoma, J. A. M. A. **91** 226 (July 28) 1928.

8 Dr. Jordan of the Lahey Clinic has divided gastric ulcers into tractable, those healing within two or three weeks with complete disappearance of x-ray niche and return to normal tonus of the stomach wall, and intractable, those which do not heal completely in two weeks. Patients with the latter condition only are operated on, about 30 per cent of those with gastric ulcers seen in their clinic. This may be a valuable method of safely avoiding such a formidable operation as resection of a gastric ulcer in many cases. However the total number of cases is not as yet large, and it is difficult, in the average situation, to obtain such accurate medical and roentgenologic study and to have patients report regularly for follow-up examination over a long period of time. See Jordan, Sarah M. Gastric Ulcer and Cancer, J. A. M. A. **93** 16 (Nov. 23) 1929.

these patients were seen by a physician only a few times in the terminal stages of the disease. Others had refused suggested complete examination.

In 5 of the 172 cases in which roentgen examination had been made the roentgenologic reports were not obtained, leaving 167 for analysis. In 67 per cent, the roentgenologist diagnosed cancer positively. In another 19.8 per cent, the diagnosis was either ulcer or cancer, ulcer and cancer, probable cancer or syphilis and cancer making

TABLE 5—Number of Persons Who Had Roentgen Examinations

	Cases	Roentgen Examination	No Roentgen Examination	No Data Concerning Roentgen Examination
Total number of cases	287	172 or 60%	84 or 29.2%	31 or 10.8%
In hospital	172	142 or 82.5%	8	22
Not in hospital	115	30 or 26.1%	76	9

TABLE 6—Results of One Hundred Sixty-Seven Roentgen Examinations of Persons Who Subsequently Died of Cancer

Results of Examination	Cases		Percentage for Comparison
	Number	Percentage	
Positive cancer	112	67.0	72.3 McVicar 0.4 and Daly
Ulcer or cancer	13	7.8	
Probable cancer	13	7.8	
Syphilis or cancer	3	1.8	
Pyloric or duodenal cancer	2	1.2	1.0 17.6 misc lesion
Cancer and ulcer of cardia	1	.6	
Cancer or ulcer	1	.6	
Total positive or suspected cancer	145	86.8	
Result negative	6	3.6	1.2
Gastric ulcer (no reference to cancer)	5	3.0	7.5
Result of 1st examination negative of			
2nd positive	4	2.4	
Duodenal ulcer	2	1.2	
Result not definite	2	1.2	
Ulcer at gastroenterostomy of stomach	1	.6	
Extragastric pressure	2	1.2	
Total misleading	22	13.2	

86.8 per cent positive or suspected cancer. In 13.2 per cent, the x-ray picture was definitely misleading (table 6).

This estimate of the accuracy of roentgenologic diagnosis of a malignant gastric condition agrees rather closely with the much larger experience in the Mayo Clinic recently reported by McVicar and Daly.<sup>9</sup> In their 1,104 cases of gastric cancer in which roentgen examination had been made, the result was positive in 72.3 per cent, compared with 67 per cent in our cases. Though further comparisons are difficult because of the difference in terms used, it is evident that there was

<sup>9</sup> McVicar, C. S., and Daly, Joseph. Diagnosis of Operable Cancer of Stomach, *Ann Int Med* 1:152, 1927-1928.

a similar small percentage in which the lesion was placed in the duodenum, a small number (smaller than in our series) in which the result of roentgen examination was negative and a larger number in which gastric ulcer was diagnosed

Twenty of the 22 cases (13.2 per cent) in which the x-ray picture was definitely misleading are detailed in table 7. In seven cases the result of the roentgen examination was negative, sometimes within one month of death from cancer. In 4 cases, one x-ray picture was negative and a second positive, in 2 of these, the cancers were in the cardiac region. In 1, the x-ray picture was not definite. In another, the cancer had perforated, and the large abdominal abscess surrounded by viscera was taken to be an extragastric neoplasm. Five cases were diagnosed gastric ulcer, in 2 of these, gastro-enterostomy had been performed, to be followed after some months by the clinical picture of carcinoma. Two cases with marked obstruction were thought roentgenologically to be duodenal ulcers. From this, it can be seen that one month before death from carcinoma of the stomach the x-ray picture can be negative. The cases in which the roentgenologist diagnosed ulcer with no noted suspicion of cancer either were at the pylorus and accompanied by obstruction (4 cases), or were ulcer craters on the lesser curvature (2 cases). The cases in which mistakes were made in the roentgen diagnosis were not preponderantly in the left half of the stomach, where no premium is placed on accurate diagnosis, but in anatomic locations where resection is possible.

The lesson taught is that, although the x-ray picture is helpful in the early diagnosis of a malignant condition, the roentgenologic diagnosis is not accurate enough to be used to the exclusion of other clinical interpretations. Given a mildly but definitely suspicious clinical history of gastric malignancy, a negative diagnosis by means of the x-ray should not entirely rule out cancer.<sup>10</sup>

#### THE CHIEF DIFFICULTIES AND ERRORS IN TREATMENT

As was noted in previous studies,<sup>3</sup> the mortality from gastro-enterostomy is about as high as that from resection. It is being appreciated lately that gastric resection, if at all feasible, is a better palliative procedure than gastro-enterostomy, patients are more comfortable following it, and patients with nodules in the liver have lived three years after gastrectomy for cancer. Also, glands in the lesser omentum are frequently inflammatory when thought to be cancerous. The problem in the treatment of persons with gastric cancer, then, is doing more gastric resections with a much lower mortality.

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10 J. C. Bloodgood (in Lewis, Dean: *Practice of Surgery*, Hagerstown, Md., W. F. Prior Company, 1928, vol. 6, chap. 8, p. 84) mentioned the possibility of a roentgenologic examination overlooking malignancy, citing two instances.

TABLE 7—*Twenty Fatal Cases of Cancer of the Stomach in Which Roentgenologic Diagnosis Was Misleading*

Cases in which result of examination by x-ray was negative (7)		
Roentgen Diagnosis		Final Condition
No 590	Dissected appendix 1 month before death	Cancer of pylorus (operation autopsy)
No 28	Negative 1 month before death	Cancer of stomach (autopsy)
No 556	Negative 1 month before death	Cancer in ulcer with metastases
No 407	Negative 1 month before death	Adenocarcinoma of lesser curvature
No 104	Negative 1 month before death	Cancer of pylorus (autopsy)
No 113	10-3-29 Stomach fills readily pyloric end pulled over to gallbladder region no filling of cap, no 5 in retention	Autopsy 10-5-29 Almost complete contraction of pyloric ring 1 cm in width, microscopically adenocarcinoma
No 200	10-16-29 Negative no evidence of gastric lesion of esophagus, stomach or duodenal bulb	Operation 1 week later, extensive cancer of lesser curvature with metastasis in lesser omentum, death, Dec, 1929
Cases in which result of 1st examination was negative, of 2nd, positive (4)		
No 302	March 1927 Negative Feb 1928 Cancer of cardiac end of stomach	
No 397	1926 Negative diet, etc prescribed Six months later Lesion of stomach	Operation, carcinoma of midportion of greater curvature
No 22	5-20-27 Perforated ulcer with no evidence suggesting cancer perforation due to extragastric pressure, 2nd x-ray picture Advanced cancer of stomach probably inoperable	
No 215	1st x-ray picture Ulcer at cardia, a malignant condition to be considered Patient then went to a nationally known clinic where although esophagoscopy showed slight suspicious lesion at the cardia, x-ray picture was negative	Operation 7 months later large cancer mass found in the cardiac region of stomach with crater in lesser curvature
Case in which x-ray picture was not definite		
No 474	Jan, 1928, x-ray picture negative stomach and duodenum cap, gallbladder suspected cholecyst diagnosis typical duodenal ulcer patient benefited with Sippy diet and rest etc May 1928 Stomach large marked by hypertrophy of angle of greater curvature	Operation 5-18-29 tumor mass size of lemon involving cardiac end of stomach
Case of extragastric pressure		
No 616	12-27 no intrinsic gastric lesion, defective shadow in greater curvature at antrum due to pressure caused by palpable tumor mass palpation revealed stomach and entire enteric tract thrown more to left on account of the mass in right upper and lower quadrants, stomach seemed fixed above mass	Operation, large abscess surrounded by intra-abdominal viscera, new growth invasion of intestines and abdominal wall microscopically adenocarcinoma of stomach degenerating
Cases in which roentgen diagnosis was gastric ulcer (5)		
No 162	Crater of large ulcer on lesser curvature, hour-glass deformity of stomach	Operation, tumor mass in stomach, liver involved
No 172	Incisure of greater curvature of stomach with slight irregularity opposite suggesting gastric ulcer	Operation tumor mass involving entire lesser curvature
No 52	Gastric ulcer, gastro-enterostomy performed	Symptoms of cancer started 1 year later
No 501	Definite defect of pylorus which is constant, dilatation of stomach, marked residue after 6 hrs, diagnosis ulcer of pyloric and duodenal junction	Massive cancer of pylorus, operation
No 525z	Gastric ulcer gastro-enterostomy performed	Subsequent modified Sippy management for epigastric distress operation 8 mo later extensive cancer of lesser curvature
Cases in which roentgenologic diagnosis was duodenal ulcer (2)		
No 400	Duodenal ulcer with obstruction	Operation, of cancer of stomach, with metastases to lymph nodes
No 506	Marked obstruction in duodenum with 50% retention in 23 hrs	Large indurated pyloric cancer

Table 8 shows that the patients with resections had symptoms for 8.1 months—1 month longer than those in whom exploration only was done, and 1.3 months less than those in whom gastro-enterostomy was done. The experience of the Mayo Clinic shows that those who had resections had symptoms longer than those who had only gastro-enterostomy or exploration. Evidently there is something in the type of growth, in addition to the duration of symptoms, which determines its resectability. The average total duration of illness of the patient with cancer of the stomach in this series was from 15 to 16 months, whether no treatment was given or whether gastro-enterostomy or exploratory laparotomy were performed. Patients with resections lived, on the

TABLE 8—*Relation of Duration of Illness and Mortality to Operation for Cancer of Stomach*

Case Series	Resection			Gastro Enterostomy			Exploration Only			No Treatment
	Cases	Duration of Illness, Mo	Mortality, %	Cases	Duration of Illness, Mo	Mortality, %	Cases	Duration of Illness, Mo	Mortality, %	Duration of Illness, Mo
Our series	28	8.1 (before operation)		35	9.4 (before operation)		29	7.1 (before operation)		
McVicar and Daly	524	10.9 (before operation)		203	8.9 (before operation)		432	8.2 (before operation)		
Cancer with sudden onset		12.0 (total cancer illness)			12.8 (total cancer illness)			16.5 (total)		
Cancer with preceding indigestion		13.5 (total)			15.0 (total)			15.5 (total)		15.5
			64			54.3			53.6	

average, two months less. The high mortality from all operations and the similar mortalities for resections, gastro-enterostomy and exploratory laparotomy are noted.

Whether a patient has his stomach resected or not may depend somewhat on the hospital environment into which he falls—surgical skill, opportunities for preoperative and postoperative care, etc. Whether more of these patients might possibly have had gastric resections is not known. Sometimes the operative notes made one wonder whether resections might not have been possible, "freely movable tumor of pylorus, gastro-enterostomy done."

*Resection*—To the 28 resections in this series, 35 additional cases were added,<sup>11</sup> making 63 for analysis.

11 The additional cases were collected from Detroit hospitals chiefly before and subsequent to the time of the aforementioned series, also from the University of Michigan Hospital, Ann Arbor, 1926-1927-1928. Dr. Fred A. Collier of the University Hospital permitted us to use the latter cases.

Table 9 shows the anatomic location of these 63 resected growths. Practically all occurred in the distal half of the stomach, the greater number in the pyloric and prepyloric regions. No resections of the proximal portion of the stomach were attempted. As noted previously, this is important practically, the resectable growths are more apt to have easily recognizable symptoms, while the inaccessible ones high up toward the cardia are those which more often start with atypical symptoms difficult to recognize.

Table 10 shows the relation of retention to postoperative death and recovery and to anatomic location (tabulating the cases in which this information was available).

TABLE 9—*Relation of Anatomic Location of Sixty-Three Resected Gastric Cancers to Postoperative Results*

	Postoperative Results	
	Deaths	Recoveries
Pylorus	8	8
Pyloric and prepyloric	8	7
Antrum	2	3
Midportion	5	3
Distal half	5	2
Lesser curvature	3	8
	32	31

TABLE 10—*Relation of Retention to Postoperative Death and Recovery, and to Anatomic Location*

Location	Deaths		Recoveries	
	Retention	No Retention	Retention	No Retention
Pylorus	5	0	6	0
Pylorus and antrum	5	2	2	8
Midportion	2	6	0	3
Lesser curvature	2	0	2	4

It is evident that

- 1 All pyloric growths were associated with obstruction when they came to operation.

- 2 Of those labeled pyloric and antral, the obstructive cases showed three times the mortality which the unobstructive did.

- 3 Growths extending to the midportion of the stomach, though showing little obstruction, nevertheless had a high postoperative mortality, probably due to the extensive and difficult resections necessary for their removal.

- 4 Growths of the lesser curvature gave rise to less obstruction, and their resection was followed by recovery of the patient in a high percentage of the cases, in this small series, they were the most favorable growths for resection. These develop on the basis of preexisting ulcer more frequently than cancers elsewhere in the stomach.



A palpable mass certainly is no contraindication to radical removal. Thirty-four of 53 charts had a note that an epigastric mass was palpable. In the remainder, this datum was not available. Eleven of twenty-six patients who recovered from resections had a palpable mass.

As few autopsies were done, it was difficult to determine the cause of death in all instances. Roughly, three groups of postoperative complications are usually distinguished: (1) abdominal complications, chiefly leakage or peritonitis, (2) circulatory failures from shock, hemorrhage, acute cardiac dilatation, etc., and (3) pulmonary and other complications.

TABLE 11—*Causes of Postoperative Death in Sixty Patients Following Partial Gastrectomy for Cancer*

	Detroit		Mayo Clinic		Total	Per Cent
	Our Series	Additional Cases	1927	1928		
Peritonitis	8	6	4	6	24	40.0
Circulatory failure	9	5	3	2	19	31.7
Hemorrhage		2				
Shock		3	2			
Cardiac failure			1	2		
Pulmonary complications	2	3	1	3*	12	20.0
Embolism		1	2	3		
Bronchopneumonia	1	1	2			
Abscess of lung	1	1				
Miscellaneous	0	3	1	1	5	8.3
Atrophy of brain				1		
Parotitis				1		
Superior mesenteric injury		1				
Perforated before operation		1				
Unclassified		1				
Totals	19	17	12*	12*	60	

\* 9.2 per cent of total number of gastrectomies for cancer.

Many charts had a specific note as to the probable cause of death. To this was added the information in the postoperative interns' and nurses' notes, a record of the temperature, the pulse record, etc. For example, A patient dying within from 24 to 36 hours with rapidly mounting pulse rate, vomiting blood, but having little pain, was thought to have died of shock or hemorrhage. One dying within the first two weeks showing continued profuse drainage from the wound, or having severe pain in the abdomen, irregular temperature and relatively normal pulse rate until shortly before death was thought to have had leakage from the suture line or peritonitis. Pulmonary complications seemed to group themselves readily in most instances by cough, rapid respirations, expectoration and freedom from postoperative abdominal complaints.

On a basis of this rough clinical interpretation, table 11 represents 60 deaths in which data about postoperative complications were obtained.

For comparison, the causes of death following gastric resection in two years' experience at the Mayo Clinic are included<sup>12</sup>

Apparently, pulmonary complications account for only about one fifth of the total postoperative mortality. Cardiac failure, hemorrhage and shock account for another third. Many of the so-called shock deaths were probably the result of alkalosis, etc., in patients who had toxemia due to retention. With the exception of a small miscellaneous group, peritonitis accounts for the remaining deaths—40 per cent. Thus, pulmonary complications and genuine myocardial failure excluded, most of the complications were "inherent in the wound itself."<sup>13</sup>

So many of these patients come to operation in an exhausted state, and so many cases of extensive and late cancers are accepted for resection that there is considerable risk because of the lowered resistance of the patient. However, a study of the charts indicates that further improvement in recoveries from operation will come with more careful preoperative preparation (repeated lavage and building up of depleted body fluids), deliberate and careful suturing and accurate hemostasis. With the newer anesthetics (spinal, local, etc.) there is not so much premium on speed in these cases, and it seems that immediate postoperative shock was more often due to hemorrhage or toxemia from a poor general condition than it was due to failure of the heart per se.

Another point which must be important is the extent of the resection. How wide of the growth is the division of tissue? A few of the patients with resections who recovered seemed to have had a local removal. The lymphatics draining the stomach are numerous, and get outside the scope of operative removal in short order. One reason for the lack of the success that gives rise to professional pessimism about cancer of the stomach—the feeling that even if the patient recovers, he is doomed to a recurrence within a relatively short time—is, perhaps, that many resections are made too close to the growth.

The case to be described seems to illustrate this.

CASE S499—An apparently satisfactory posterior Polya resection of a large prepyloric gastric cancer was done, with good postoperative recovery. After twenty-five months' freedom from the condition, the patient was admitted to another hospital with signs of obstruction at the cardia, from which he died, the clinical diagnosis being inoperable carcinoma.

<sup>12</sup> Personal communication to the authors from Dr Donald A. Balfour.

<sup>13</sup> As stated, this is only a rough interpretation from a study of postoperative records. Dr Balfour<sup>12</sup> notes that pulmonary complications and peritonitis may both be found as the cause of death. A small local peritonitis, not of itself sufficient to cause death apparently, may be the only observation at autopsy.

The pathologic report from the first institution contained the note "All of the stomach wall sent us shows diffuse (cancerous) infiltration to the serosa"

The query, in retrospect, is If the patient died of recurrence at the cardia, would an anterior Polya resection and anastomosis which might have allowed more of the wall of the stomach to be resected have been better insurance against recurrence?

#### POSSIBILITIES FOR IMPROVEMENT AND CONTROL

It is evident where improvement will come

1 It is not appreciated that a mild indigestion, starting suddenly in persons of middle age, if unrelieved by only a few weeks' treatment, warrants surgical exploration for so serious a condition as suspected gastric cancer. The concept is so unusual as regards the average consideration these patients get that it must be grasped as a new clinical entity by most physicians before much headway in control will be in evidence.

In this stage, the clinical history of the illness is the all important element. The knowledge that gastric ulcer is not common, the knowledge of the earmarks of cancerous indigestion, the knowledge that in many cases there are no earmarks, the probable error in the clinical confusion of ulcer and cancer are more important than the physical examination, the laboratory data or even the x-ray picture. It is probably not wise to urge people to suspect cancer of the stomach if they have mild indigestion until there is improvement in the clinical recognition of early gastric cancer.

2 Although the diagnosis is based in most instances on the roentgenologic examination, there is a certain element of error that must be appreciated.

3 Though much of the mortality from gastric resections is due to the weakened state of the patients, improvement will probably come chiefly from careful preoperative preparation and care in hemostasis and suturing.

#### SUMMARY AND CONCLUSIONS

1 The popular pessimism concerning cancer of the stomach is well founded. Perhaps 3 per cent of the total number of persons who have died from gastric cancer have had the growth resected and recovered from the operation—have had the chance of cure that operative recovery from radical resection represents.

2 Of 287 fatal cancers of the stomach, 24.7 per cent were preceded by long continued indigestion, 75.3 per cent started suddenly from previous good health.

3 Of those which started suddenly from previous good health, 69 per cent started with symptoms which, though mild, were distinctly referable to a pathologic disturbance in the upper part of the abdomen. The chief problem is not the recognition of symptoms, but the arousal of suspicion that they may be of serious import.

4 Cancers that start with atypical symptoms are more apt to be in the left half, the nonresectable portions, of the stomach than toward the pylorus.

5 In the arguments concerning the frequency with which chronic gastric ulcer develops into gastric carcinoma, the fact may be lost sight of that it is not the frequency with which this takes place, but the difficulty of distinguishing clinically gastric ulcer from early carcinoma which is important. One third of the 25 per cent of these patients who had had long continued indigestion had been given the diagnosis "typical ulcer history", one half of these had been under medical management for ulcer. Ten per cent of the remaining patients whose cancers started from preceding good health were noted as having a history typical of ulcer.

6 Twenty-six per cent of the patients who had not been in hospitals had had roentgen examinations.

7 There is a definite though small error in roentgenologic diagnosis of cancer even when the growth is well developed. With a mildly but definitely suggestive clinical history of a malignant gastric condition, a negative x-ray picture should not entirely rule out cancer.

8 The problem as regards treatment is doing more gastric resections (since the mortality from gastro-enterostomy is high and a successful resection, if at all feasible, is a better palliative procedure than is gastro-enterostomy), and doing them with a lower postoperative mortality.

9 Concerning the deaths following gastric resections for carcinoma, it may be said, in a rough clinical interpretation, that 20 per cent were thought to be due to pulmonary complications, one third were due to circulatory failure, a small number of these cardiac failure per se, the larger proportion shock due to hemorrhage or toxemia from retention and dehydration, and 40 per cent were due to peritonitis.

# CHRONIC SUBDURAL HEMATOMA

SUMMARY AND ANALYSIS OF FORTY-TWO CASES COLLECTED FROM  
THE LITERATURE, WITH REPORT OF TWO ADDITIONAL CASES \*

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Prior to the publication of Putnam and Cushing<sup>1</sup> in 1925, great confusion prevailed as to the nomenclature and classification of hemorrhage beneath the envelops of the brain. Hemorrhage beneath the pia, arachnoid and dura and above the dura, as well as into the brain substance itself, was often loosely designated as pachymeningitis hemorrhagica or simply as intracranial hemorrhage. These authors brought order to a division of this chaotic literature by establishing hematomas between the dura and arachnoid as a definite clinical entity. Since their report, numerous studies and case reports have appeared in the literature.

In the treatment for traumatic cases of the head, the prognosis often depends on the recognition of the exact abnormal condition present within the skull. For instance, it makes a great deal of difference in treatment whether there is a cerebral laceration or contusion, diffuse subarachnoid hemorrhage or a clot beneath or above the dura mater. While the symptoms of subdural hematoma have been enumerated in previous contributions, no statistical study of the prominent symptoms associated with this malady has been made. Therefore, I have carefully selected from the literature forty-two confirmed cases of chronic subdural hematoma and have attempted to analyze the signs and symptoms presented by each, in order to consider them collectively and determine the most characteristic features as indicated by their frequency of occurrence. This information is presented in table 1.

## ANALYSIS OF CASES

I am aware that the number of cases summarized in table 1 is not sufficiently large to allow one to select the exact observation in the average case of chronic subdural hematoma, yet it is considered better to analyze fewer cases of confirmed lesions than many cases with indefinite lesions and incomplete records. It is believed, however, that

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<sup>1</sup> Submitted for publication, Jan 20, 1930

\* From the Neurological Service of the Department of Surgery, Louisville City Hospital and University of Louisville, School of Medicine

1 Putnam, Tracy Jackson, and Cushing, Harvey. Chronic Subdural Hematoma, Arch Surg **11** 329 (Sept) 1925

the statistics arrived at may be taken as characteristic of the condition under consideration and may serve as a guide for further study. The analysis has been made from the point of view of incidence, etiology, symptomatology, morbid anatomy and treatment.

*Incidence*—It is interesting to note that in the cases mentioned, as shown in table 2, the incidence is fairly constant after the second decade, while the average age of patients is 39.2 years. Seven per cent occurred in females, while 93 per cent occurred in males. The condition is not rare among children. Schwartz,<sup>2</sup> and also Burhans and Gerstenberger,<sup>3</sup> reported several cases occurring in childhood.

*Etiology*—A review of the various predisposing and determining factors will not be considered here. Putnam<sup>1</sup> reviewed the literature thoroughly in this connection and concluded that trauma is the only single antecedent factor common to all cases. In only one case of my collection, that of Rosenbaum, was it definitely stated that trauma had not occurred. No history of any kind was obtainable in two, no mention of trauma was made in two more. Eighty-eight per cent had definite history of trauma, while 98 per cent may well have been traumatic, and only 2 per cent gave a history of no trauma having occurred. Only twenty-five per cent received sufficient injury to produce unconsciousness.

*Symptomatology*—There is an extreme variability of symptoms. A picture of the condition usually exists in the rough, but it is seldom that a clearcut, well rounded out picture of an intracranial lesion will develop. The details are sometimes as conspicuous by their absence as by their variety.

Dunn<sup>4</sup> defined and described a group of symptoms which he regarded as pathognomonic of the disease. Generally there is a latent period lasting from a few days to several years, then headache followed by psychosis and later coma.

As an aid to the establishment of a definite clinical picture and better recognition of this condition, the frequency of the various signs and symptoms has been determined and a classification of the major and minor symptoms made.

*Latent Period*—This is the quiet period extending from the time of injury to the onset of symptoms. It was definitely present in 70 per cent of the cases mentioned. Its average length was seventy-six days in thirty-one cases, while only twenty-five days if two of the particularly long cases were excluded.

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2 Schwartz, A. B. The Etiology of Pachymeningitis Hemorrhagica Interna in Infants, *Am J Dis Child* **11** 23 (Jan) 1916.

3 Burhans, C. W., and Gerstenberger, H. J. Internal Hemorrhagic Pachymeningitis in Infancy, *J A M A* **80** 604 (March 3) 1923.

4 Dunn, A. D. Pachymeningitis Hemorrhagica Interna, *Am J M Sc* **163** 819, 1923.

TABLE 1—Analysis of Signs and Symptom

Reported by	Age	Sex	Latent Period	Lucid Interval	First Symptom	Headaches	Mental Changes	Vomiting	Drowsy	Motor	Cranial Nerves	Reflexes	Eyes, Fundi
Cushing <sup>1</sup>	68	F	3½ hours		Headache	Yes	Yes			Impaired on right side			Left obscure
Putnam <sup>1</sup> I	18	M				Yes	Yes	Yes	Yes	Right hand awkward	Weakness of left 6th	Right deep exaggerated, right abdominal absent	3 diopters choking, bilateral
II	32	M	5 weeks		Headache	Yes (left)	Yes		Yes	Right hand weaker than left	Slight anosmia	Knee reflex, right greater than left	1 diopter choking, bilateral
III	58	M	10 days		Headache	Yes	Yes		Restless	Incontinent		Deep reflexes on right side greater than on left	Left disk blurred
IV	38	M	2		Headache	Yes	Yes	Yes	Yes			Knee reflex absent, others sluggish	Converged left, diplo
V	57	M			Drowsy, headache	Yes (left occipital)	Yes			Twitching of right arm motor aphasia, (left handed)			Papilledema right pupil larger than left
VI	58	M	4 mos	5 mos		Yes	Yes			Paralysis of left arm		Babinski, left	Choking of right hemisphere, atrophy
VII	46	M	2 weeks		Weakness, right leg	Yes	Yes	Yes	Yes			Biceps increased on right, right achilles increased	3 diopters choking, bilateral, vision impaired
VIII	34	M	3 mos		Headache	Yes, (occipital)	Yes	Yes	Yes		Diplopia		Bilateral choked disk
IX	50	M	8 wks	10 wks	Headaches	Yes (right occipital)	Yes		Yes	Left arm and leg weak, spasticity, left	Left 7th weak		Papilledema left pupil larger than right
X	64	M	1 year		Headaches	Yes					Taste impaired		Left pupil larger than right bilateral choked disk
2d admission	34	M		30 mos			Yes		Yes	Left side more spastic than right		Bilateral ankle clonus left Babinski and Oppenheim	
XI	20	M			Rhinorrhea		Yes		Yes				Old atrophy of disks
Pickens, C B Guy's Hosp Rep 78 365, 1928	64	M	1 mo	1 mo	Headaches	Yes	Yes	Yes	Yes	Right spastic hemiplegia, incontinence		Increased on right side, abdominal absent	Engorgement of veins
West, E M B Guy's Hosp Rep 78 474, 1928	49	M				Yes (occipital)	Yes			General loss of motor power	3, 4, 6, bilateral weakness right 5, 7, 9, 12 paresis	Right corneal absent right abdominal absent, knee reflex, right greater than left	
Craig, W M S Clin North America 7 1523, 1927 I	41	M	1 mo		Drowsy	Yes	Yes	Yes	Yes	Rigidity of right arm greater than left, incontinence	Weakness left 7 and 3 bilateral	Bilateral Babinski	2 diopter choking left 3 diopter choking right

# *ty-Two Cases of Chronic Subdural Hematoma*

ative or ry b va ns	Tem pera ture	Pulse Rate	Coma Yes	Renu sion Yes	Injury			Hematoma		Corte x De formed	Blood Pres sure	Results
					Type	Region	Objective Symptoms	Region	Consis teney			
		50		Yes	Fell on floor	Right parietal		Right parietal	Semi fluid			Operated on, du
				Yes	Foot hall			Left fronto parietal	Clot fluid	Com pressed		Operation, reeo good
ary min	100.4 (38 C)	46		Yes	Auto accident		Confusion over eye	Left hemi sphere	Clot fluid	Flat tened		Ventriculogram flap, subarachno drain, recovered
ary ( white red cells	102.2 (39 C)	Slow			Auto accident	Occipital	Laceration of scalp, unconscious	Left hemi sphere	Clot	Flat tened		Recovered, explo tory puncture drain reelevatio and no clot
				Yes	Struck with ball	Right parieto occipital		Right parieto occipital	Clot fluid			Recovered, vent gram, ventricles right
			Yes	Yes				Bilateral	Fluid clot	Flat tened	123/90	Right flap died
			Yes	Yes	Thrown from ear	?	?	Right temporo parietal	Fluid clot	Com pressed	100/60	Subtemporal dee pression, second operation, died
		72		Yes	Kicked by colt	Left side of head	Uncon scious	Left parietal	Fluid clot	Com pressed	118/70	Ventriculogram eration rongcur bone 2 inches in eter removed d no postoperative exacerbation
		74	No	Yes	Fell on ice		Uncon scious	Left temporo parietal	Clot	De pressed	116/64	Ventriculogram with decompressi recovery
		70	Yes	Yes	Struck	Right side of head	Uncon scious	Right parietal	Clot fluid	Com pressed		Flap relevation and dura remov drain, recovery
	Sub normal			Yes		--		Left temporal	Fluid		110/70	Decompression, 1 18 months
no e od	100.04 (37.8 C)			Yes	Fell from pier	?	Uncon scious, laceration of scalp depression of frontal	Right frontal	Fluid	Com pressed		Right cyst drain same day flap re elevated and pa died
				Yes	?	Head		Right hemi sphere	Clot			Flap, ventriculo recovered
od a ig	Sub normal	Slow	Yes	Yes	Slipped, struck head	Occiput		Left pos terior fossa		Com pressed	140/55	Died no operati
oa sser in itive		96		Yes	?	?	?	Right occipito parietal	Fluid	Flat tened	105/65	Died, no operati
oo te od s			Yes	Yes	Struck head on horn			Right temporal	Clots fluid	Normal		Recovered oper



TABLE 1—Analysis of Signs and Symptoms in Fort 1

Reported by	Age	Sex	Latent Period	Lucid Interval	First Symptom	Headaches	Mental Changes	Vomiting	Drowsy	Motor	Cranial Nerves	Reflexes	Eyes, Fundi
Craig, W M II	Continued 30	M	3 mos		Headaches	Yes, (occipital)		Yes	Yes		Diplopia		Bilateral choking of disks with hemorrhage
III	46	M	2 weeks		Weakness of right leg and knee	Yes (frontal)	Yes	Yes				Right biceps increased, necks increased, bilateral	Bilateral choked disk with hemorrhage and exudate
IV	14	M			Headaches	Yes (vertex)				Adidokokinnesia of left forearm left lower extremity incoordinated		Babinski and Kernig positive, left	1 diopter cataract, bilateral with hemorrhage and exudate
V	21	M	3 mos		Dizziness	Yes (right occipital)	Yes	Yes	Yes	Diplopia, residual paralysis of left leg opisthotonos		Achilles bilateral, increased	3 diopters choked bilateral
Rosenbaum, H A Arch Pediat 46 56, 1929	9 wks	M			Twitching, right side		Yes	Yes	Yes	Trembling of right leg and arm		All increased	
Grant, F C Ann Surg 86 485, 1927	52	M	10 days		Headaches	Yes	Yes		Yes	Weakness of right extremities	Weakness right 7	Reduction of all reflexes	Margins blurred bilateral
II	67	F			Headaches	Yes (occipital)	Yes	Yes	Yes	Weakness of right extremities	Weakness right 7	Plantar reduced on right, increased on left Babinski left	
III	43	M			Buzzing in ears and dizziness	Yes	Yes		Yes	Twitching of right side of face and right arm	Right 7 weak	All exaggerated bilateral Babinski	Vessels full and tortuous
Bondurant, E D Alienist & Neuro 14 1, 1893	41	M			Drowsy		Yes		Yes	Left hemiplegia (incomplete)	Right 7 in complete		
Griswold and Jelsma Arch Surg 15 45, 1927	46	M	8 days 9 wks		Headaches	Yes	Yes		Yes			Increased right upper extremity knee reflexes exaggerated bilaterally	
II	66	F	4 days 9 days		Dispondent		Yes		Yes	Contractures of toes, right	Lower left 7 weak left 12 weak	Patellar increased on left	
III	54	M	32 days 2 mo		Headaches, weakness	Yes	Yes	Yes	Yes			Abdominal absent all increased on right side	

*Cases of Chronic Subdural Hematoma—Continued*

Positive Laboratory Observations	Temperature	Pulse Rate	Consciousness	Remission Yes	Injury			Hematoma		Cortex	Blood Pressure	Recovered, Recovered,
					Type of Injury	Location ?	Objective Symptoms Unconscious	Location	Consistency			
		72			Kicked by colt	Left side	Unconscious	Right parietal	Clot fluid		118/70	Recovered
		Slow		Yes	Wrestling			Right parietal	Clot fluid			No operative
				Yes	Struck floor	Occipital	Unconscious	Right temporo parietal	Clot	Medullary hernia		Died, no medullary
		101		Yes	No injury			Right and left parietal	Fluid			Subdural recovery
	Sub normal		Semi conscious		fell down stairs		Fractured clavicle	Left temporo parietal	Clot and fluid	Com pressed yellowish green	150/80	Flap recovery
Primary bunton		60	Yes		fell from ladder	Left occipital	Incision of scalp	Left temporo parietal to occipital	Clot fluid	Flat tened, anemic	120/70	Recovered
	Normal	Slow	Yes	Yes	Bathing in heavy sea		?	Left temporo parietal	Clot	Flat tened anemic		Trephine, but
				Yes	Yes	Munroe	?	Right and left	Clot			Died no operative
	Normal	90	Yes	Yes	Auto struck patient	Left frontal	Not unconscious, left frontal laceration	Left hemisphere	Clot	Normal	120/80	Died, no operative
	99.4	105	Yes	Yes	fell	Left frontal	Hematoma in left frontal region	Right temporo parietal	Clot liquid	Yellow tinged	180/105	Died no operative
	98.6		Yes	Yes	Struck head against door	Left frontal	Unconscious	Left hemisphere	Clot	Flat tened and discolored	170/90	Died no operative

TABLE 1—*Analysis of Signs and Symptoms in Forty T*

Reported by	Age	Sex	Latent Period	Lucid Interval	First Symptom	Headaches	Mental Changes	Vomiting	Drowsy	Motor	Cranial Nerves	Reflexes	Eyes, Fundi
Griswold and Jelsma—Continued	40	M			Headaches	Yes	Yes		Yes	Weakness of right side, left arm twitched	Left 7, supra nuclear, left 12 weakness	Tendon reflexes hyperactive, Babinski, Oppenheim and ankle clonus, right, positive	
V		M				Yes	Yes		Yes	Both upper extremities flaccid	Right pupil contracted and fixed, left dilated and fixed	Knee reflexes and biceps absent bilaterally, Babinski positive, bilateral	Hemorrhage left
Bowen, W. H. Guy's Hosp Rep vol 59, p 4	24	M	1 day		Headaches	Yes (frontal and occipital)	Yes		Yes	Intermittent paralysis of right arm with rigidity, aphasia	Blind		
II --	62	M		14 days	Right pupil dilated		Yes		Yes				Right pupil dilated
III	56	M	1 day		Paralysis of left arm and leg					Paralysis left extremity			
IV	21	M	6		Convulsions	Yes				Convulsions left arm weak			
X		M	16 days		Headaches	Yes	Yes		Yes	Slight spastic paresis, right extremity aphasia	--		
XII	18	M	11 days		Headaches	Yes	Yes		Yes				
XVI	16	M	11 days	12 days	Drowsy	Yes	Yes		Yes	Twitching upper extremity, aphasia			Right pupil dilated
XXI	23	M	Fortnite	3 wks	Headaches	Yes	Yes		Yes	Weakness right arm and leg convulsions			Pupils dilated
XXII	53	M	7 wks		Dragging of right foot					Weakness right side of body			Bilateral papilledema
XXIII	21	M	1 week		Fever and unconsciousness	Yes	Yes	Yes	Yes	Aphasia and paraphasia, partial paralysis	Weakness right 7 and 12		
XXIV	60	M	3 days	22	Headaches	Yes		Yes	Yes	Paralysis right arm and leg, weakness on left			
Hensehen, K Arch f Klin Chir 99 • 67, 1912	2	M	9 days		Convulsions, left					Clonic convulsions left, right extremities dorsiflexed	Left 6, right 3 weak		Right pupil larger than left both dilated and fixed
II	29	M	15 days	16 days	Convulsions		Yes		Yes		Left 6, right 3 weak		Right pupil larger than left
Kasemeyer, E Post traumatic meningo-		M	3 yrs	7 yrs	Weakness	Yes	Yes		Yes	Right side convulsions aphasia		Abdominal changeable	Vision blurred

*Cases of Chronic Subdural Hematoma—Continued*

Positive Laboratory Observations	Temperature	Pulse Rate	Coma Yes	Remission Yes	Injury			Hematoma		Cortex Flat- tened	Blood Pressure	Result
					Type Not known	Region	Objective Symptoms	Region	Consistency Clot			
	98.6							Entire left hemi- sphere				Died, no operation
	Normal			Yes	Unknown	?	/	Left hemi- sphere	Clot	Depressed		Died, no operation
	99	76		Yes	Struck by engine	Occiput	Unconscious 3 scalp wounds, 2 in vertex, laceration	Left pa- rietal	Clot and fluid			Complete recovery, no operation, no
	99	Normal	Yes	Yes	Struck right side of head against stone	Right side	Right tem- poral lacer- ation un- conscious	Right tem- poral	Clot fluid	?		Operation
	99.2	80			Fell, struck head	Occiput	Scalp lac- eration	Precentral and frontal, right	Clot	De- pressed		Died, found clot at autopsy
Primary dementia	102	100		Yes	Fell down stairs	/	Laceration of scalp	Right pa- rietal	Fluid	Normal		Operation
	100	92			Struck by brick	Head ?	Dazed		Clot	Normal		Recovered, dis-
					Fight- ing	Head	None	Right hemi- sphere	Fluid clot	De- pressed		Died, no operation
Incubated	101.6		Yes	Yes	Fell on curb stone	Left occiput	Laceration of scalp	Right hemi- sphere	Fluid clot			Died, no operation
Incubated	105	120	Yes	Yes	Struck on head	Left temporal	Laceration, left tem- poral	Left tem- poral	Fluid clot			Recovered, dis-
		70		Yes	Struck by brick	Left side of fore- head	Laceration of left side of forehead	Left pa- rietal	Clot fluid			Recovered, dis- covered horse hair
	101	Slow	Yes	Yes	Fell	?	None	Left hemi- sphere	Clot fluid			Recovered, dis- covered horse hair
	98.6	70	Yes	Yes	Struck by fall- ing ladder	Right temporal	Contusion of scalp	?	Clot bloody fluid			Recovered, dis-
	99	160		Yes	Fell from table	Occiput	Uncon- scious tenderness	Right hemi- sphere	Fluid			Trephined, packed, recovered
	98		Yes		Fell from ladder	Right temporal	Convul- sions	Right pa- rietal	Fluid			Trephined, packed, recovered
				Yes	Fell and struck head			Right tem- poro- parietal	Clot			No operation, autopsy

**Lucid Interval** The lucid interval is the entire period between the injury and the onset of unconsciousness. Coma was noted in 45 per cent of the cases. The length of the lucid interval could be figured in fifteen cases, the average being 264 days, however, omitting two protracted cases, the average is reduced to 35.3 days. This is ten days longer than the average for the latent period, meaning that ten days was the average length of time elapsing from the onset of symptoms until coma developed. On the other hand, there were seventeen cases in which the patient remained conscious.

**Headaches** Headache appears to be one of the most common observations, occurring in 79 per cent. Forty-eight per cent of the total number of patients stated that headache was the first symptom noted. It seems that it occurs in an insidious manner, continually but gradually increasing until some patients are driven almost to desperation just before the psychosis occurs. Seldom is relief secured by drugs, even though the patient may take excessively large quantities.

TABLE 2—*Age Incidence*

Years	Number of Cases	Percentage
0 to 10	2	4.8
10 to 20	4	9.7
20 to 30	7	17.0
30 to 40	6	14.6
40 to 50	8	19.5
50 to 60	8	19.5
60 to 70	6	14.6

**Mental Changes** Mental changes simulating those accompanying lesions of the frontal lobe, occurred in thirty-eight, or 86 per cent. Bowen<sup>5</sup> thought it improbable that subdural hematomas lead to ultimate insanity. Instead he contended that hemorrhages found in the insane are the result of atrophy of the brain associated with mental changes. Robertson<sup>6</sup> likewise did not think hemorrhages to be the cause of insanity, however, instead of being the results of atrophy (as suggested by Bowen), he expressed the belief that they are due to congestion occurring in insane patients. Hemorrhages are more often found in parietic and alcoholic psychopathic patients, and hyperemia of the dura is more frequent in these patients than in others.

Seventy-nine per cent of the patients mentioned complained of drowsiness that deepened into coma in 57.1 per cent.

Motor disturbance was noted in 70 per cent, of these, 29 per cent were spastic, 32 per cent had weakness only, 16 per cent had complete

<sup>5</sup> Bowen, W. H. Traumatic Subdural Hemorrhage, *Guy's Hosp Rep* 59:4, 1905.

<sup>6</sup> Robertson, G. M. The Formation of Subdural Membranes or Pachymeningitis Hemorrhagica, *J Ment Sc* 39:203, 1893.

paralysis, 12 per cent had twitchings and 19 per cent had motor aphasia. Fifty-six presented alteration in reflexes, particularly of the deep group.

The cranial nerves were involved in 47 per cent of the cases. Within this group the olfactory, the fifth, the chorda tympani and the ninth nerves were involved in 5 per cent, the ciliary part of the third in 36 per cent, some of the extra-ocular muscular group in twenty-six per cent, the abducens in 21 per cent, the supranuclear portion of the seventh in 26 per cent, and the infranuclear portion of the seventh in 26 per cent. The seventh nerve was involved in 57 per cent of the cases with disturbance of the cranial nerve. The trochlear was involved in 10 per cent and the hypoglossal nerve in 15 per cent.

Remission of symptoms constitutes the remaining important observation, and occurred in 84 per cent of cases.

There is a difference of opinion as to whether remissions are caused by successive hemorrhages or by the brain compensating for the increased pressure resulting from the clot. These factors may be important if chronic subdural hematoma is attributed to pressure, which is an important factor in many cases, while in many others the intracranial pressure is not increased and in a still larger number it is not equal to that necessary to produce death in other lesions, as in the case of new growths. There may be another factor, perhaps chemical, resulting from the clot, which exerts a lethal effect.

The group of symptoms given constitutes the factors which may be termed major symptoms, while those which follow may be classed as minor symptoms.

Vomiting was noted in 29 per cent, nystagmus in 11 per cent and sensory disturbance in 12.5 per cent. The pulse rate was found to be below 60 in 18.16 per cent and above 100 in 9 per cent. In 13 per cent, the temperature was above 100 F while in 6 per cent it was subnormal. Irregular respiration was noted late in the course of the disease in 11 per cent of the fatal cases. The ophthalmoscopic observations revealed hemorrhages into the retina in 11 per cent of the cases, papilledema or choked disks in 40 per cent and engorgement of vessels alone in 4 per cent. In regard to laboratory observations, 68.1 per cent showed leukocytosis, 13 per cent albumin in the urine and 13 per cent xanthochromic spinal fluid. Roentgen examination revealed fracture in 4.5 per cent of the cases.

*Morbid Anatomy*—Hematoma. W. H. Holmes<sup>7</sup> stated that all other intracranial hemorrhage is arterial, but this is venous and results from tearing a small vein which enters the tributaries of the longitudinal sinus. Bowen<sup>8</sup> gave as the probable origin of the blood (1) the main

<sup>7</sup> Holmes, W. H. Chronic Subdural Hemorrhage. *Arch. Neurol. & Psychiat.* 20: 162 (July) 1928.

arteries entering the skull, of which he had two cases, (2) meningeal vessels, of which he had two cases, (3) sinuses of the dura, of which he had three cases, (4) vessels of the pia, and (5) cerebral vessels. He considered the pial vessels the most frequent source.

Langer and also Mittenzweig,<sup>8</sup> reported the presence of veins in the parietal region far from the sinuses from which the hemorrhage may occur. In one case<sup>9</sup> of the foregoing group, examination at necropsy seemed to point to the middle meningeal artery as the origin.

In 34 per cent of the foregoing cases the location of the trauma as well as that of the clot was known. Of these, the clot was found on the same side as the trauma in 80 per cent and on the opposite side in 20 per cent.

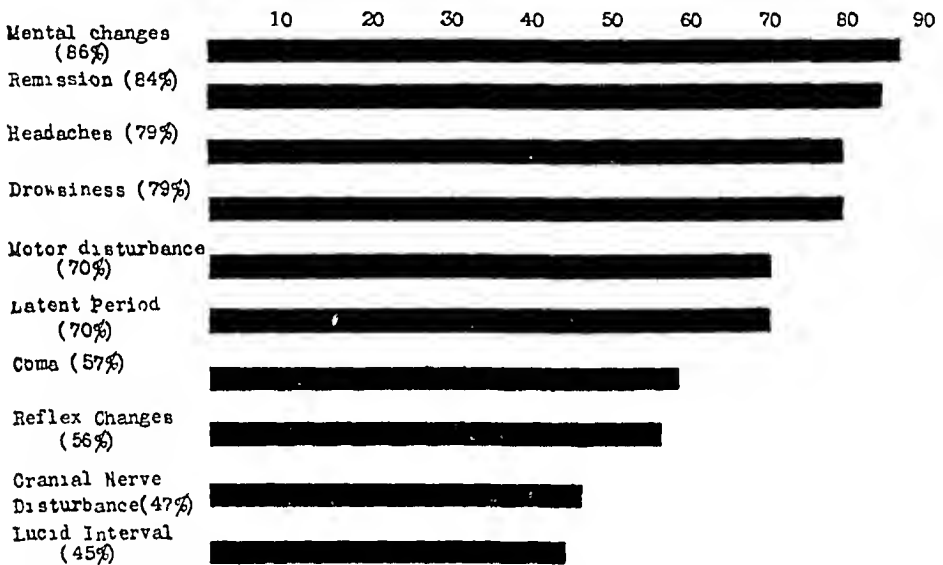


Chart 1—Incidence of major symptoms expressed in percentages (forty-two cases)

Bile pigment was noted in 69.3 per cent of the hematomas examined. From the high concentration of bilirubin,<sup>9</sup> as previously determined, along with the work of Essick<sup>10</sup> and later that of Weed<sup>11</sup> in regard to the cells of the arachnoid, it may well be said with Rich<sup>12</sup> that the

<sup>8</sup> Mittenzweig, quoted by Putnam and Cushing (footnote 1)

<sup>9</sup> Griswold, R. A., and Jelsma, F. The Relationship of Chronic Subdural Hematoma and Pachymeningitis Hemorrhagica Interna, Arch Surg **15** 45 (July) 1927

<sup>10</sup> Essick, C. R. Formation of Macrophages by the Cells Lining the Arachnoid Cavity in Response to the Stimulus of Particulate Matter. Contributions to Embryology, Carnegie Inst Contrib, Wash 1920, IX, No 272, 377-388

<sup>11</sup> Weed, L. H. The Cells of the Arachnoid, Bull Johns Hopkins Hosp **31** 343, 1920

<sup>12</sup> Rich, A. R. The Formation of Bile Pigment, Physiol Rev **5** 182 1925

meninges appear to be an exceptionally favorable site for crystallization of a bile pigment within living cells

The older the case, the more completely the clot will be organized. The likelihood of successive hemorrhages and the importance of this theory have never been established. Lamination of the clot was used as argument for successive hemorrhages, but Putnam<sup>1</sup> stated that Wigglesworth reported lamination of a hematoma formed by a single hemorrhage. It is also known that the clot does not organize evenly throughout. Fifty-four per cent of the hematomas consisted of liquid matter as well as clot, 37 per cent were thoroughly clotted and 13 per cent were practically wholly fluid.

**Cerebrum** The intracranial pressure is often increased. Cases have been reported in which the brain was compressed for six weeks

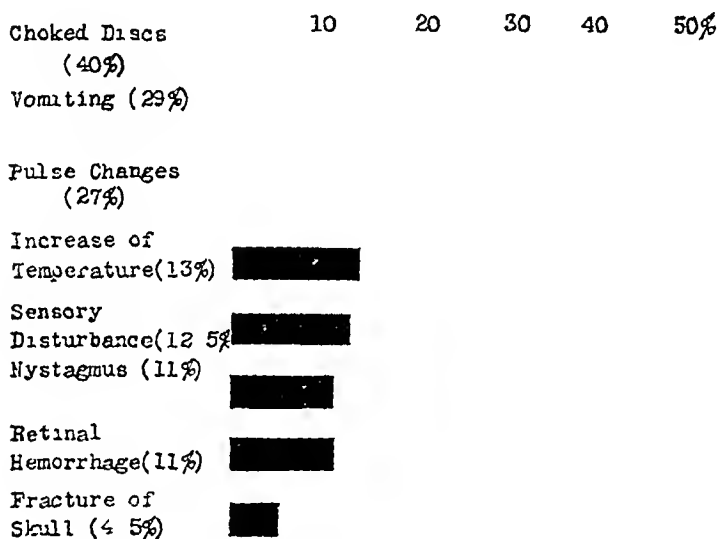


Chart 2—Incidence of minor symptoms expressed in percentages (forty-two cases)

or more, with perfect recovery. McBurney<sup>13</sup> reported a clot of seven years' duration with the gray matter gone and palsy. Usually the depressed, and often discolored, cortex is not injured grossly or microscopically, regains its normal contour and begins to pulsate shortly after removal of the clot is effected.

**Treatment**—Palliative treatment in these cases seems to be of little avail. Massive doses of drugs have been taken for the headaches, with little or no relief. Spinal punctures have been performed and intravenous hypertonic solutions have been given, but only temporary remission of symptoms has been secured.

<sup>13</sup> McBurney, quoted by Bowen (footnote 5)



The operative results have been most favorable. As soon as the diagnosis has been made, plans for the removal of the clot should be made at once.

Localization of the clot can most often be made by the focal symptoms, and every means should be employed to do so before operation. Bilateral exploration by means of burr holes and dural punctures has been of great value, is less dangerous, is more easily performed, causes less delay and affords more desirable inspection than by ventriculograms. If no information is secured by this means, a ventricular estimation or a ventriculogram may readily be secured through one of the cranial dural punctures already made.

Whether or not an osteoplastic flap or decompression openings should be employed depends on the condition of the patient. The osteoplastic flap seems preferable if more time may be used and the patient is able to stand the increased manipulations. Bernard Sachs and Elsberg<sup>14</sup> raised an osteoplastic flap twenty days after performing a decompression, with incomplete removal of the clot. Putnam<sup>1</sup> reported good results from the simple drainage of fluid, with no attempt to remove the clot. It would seem a good principle to do whatever the patient is able to stand in order to remove as much of the clot as possible. Oozing and bleeding are not marked, so the field can usually be left dry. Drains were used in 17 per cent of the foregoing cases.

Spinal punctures and intravenous injections of dextrose, 50 or 60 per cent, are of value to combat the postoperative edema during the first three or four days.

In this series, 77 per cent of the patients came to operation, 83 per cent of those with operative cases recovered.

#### ADDITIONAL CASES

*CASE 1—Traumatic subdural hematoma with onset of symptoms six days after trauma, psychosis, coma. Bilateral burr holes, osteoplastic flap, removal of clot, decompression and recovery.*

B. T., a negro, entered the hospital in a semicomatose state on Sept. 15, 1928. The history as secured from his wife was that he had been drinking freely until the time of injury. Two weeks before admission, the patient returned home intoxicated, with evidence of having received a blow in the occipital region. At this time he also fell against the stove and received an additional injury on the right side of his head. He continued to work as usual until six days later, when he began to complain of pain in the right side of his head with a severe generalized headache. The headache was unrelenting, so the patient sought relief by taking large quantities of a proprietary opiate which he bought at the drug store. About ten days after injury, relatives noted a definite change in his mental

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<sup>14</sup> Sachs, Bernard, and Elsberg, C. Extensive Subdural Hematoma After Trauma, *New York M. J.* **104**: 633 (Sept. 30) 1916.

attitude Three days later (September 13), the patient returned home irrational, and the next morning he was found unconscious in bed At the time of admission, he was in a semicomatose state, his pulse rate was 44, strong and full, the temperature was 100 F, and respiration was 60 The coma gradually became more profound The results of a general physical examination were negative The original site of trauma had healed

The right pupil was fully dilated There was slight deviation of the right eye externally, eye movements could not be elicited The optic fundi were normal As far as could be ascertained, the other cranial nerves were normal

There was a spasticity of the left side of the body, including the upper and lower extremities Twitchings of the left arm were noted The right side of the body and the extremities were flaccid (This was interpreted as being natural because of the comatose state) The deep reflexes were exaggerated on the left side The abdominal reflexes were absent There was no ankle clonus, Gordon's sign or Oppenheim's sign

The laboratory observations were largely negative The urine was normal The blood showed white blood cells, 11,000, polymorphonuclears, 84 per cent The spinal fluid was xanthochromic and under normal pressure, with 15 cells, 8 lymphocytes and 7 polymorphonuclears A trace of globulin was found Cultures of the spinal fluid were negative The chemical analysis of the blood was negative Roentgenograms revealed no fracture of the skull

A diagnosis of "subdural hematoma" was made, and immediate operation was planned With the patient under local anesthesia, a burr hole was made in each temporoparietal region, and the dura was opened Nothing was found on the left side

An osteoplastic flap was turned on the right side The dura was fairly tense and of a greenish-brown hue It was opened freely, and a clot covering the entire hemisphere, about 3 to 4 mm thick in some places, was removed

A glistening membrane enveloped the clot It was attached to the dura but not to the arachnoid The center was of a semiliquid consistency Before the entire clot had been removed, the patient regained consciousness and talked The subdural space was lavaged carefully, and all particles of the clot were removed The brain was only slightly compressed, it pulsated freely The dura was closed with a gutta percha drain to the arachnoid (This was removed in forty-eight hours, and little drainage was noted) A subtemporal decompression was performed, and the flap was replaced

Section showed a partially organized clot The outer portion attached to the dura was composed of fibrous tissue Many well formed capillaries were scattered throughout the layer and large endothelial-lined spaces, some of which contained red blood corpuscles, were side by side beneath the dura There were many mononuclear leukocytes, with deposits of greenish granules in their cytoplasm A moderate amount of homogeneous, stained, granular material resembling calcium deposits was found throughout the organized tissue A single layer of flattened cells on a thin layer of fibrous tissue covered the inner confines of the clot

Convalescence was uneventful, except for headache on the second and third days The temperature, which had ranged to 102.4 F before operation, receded rapidly and remained normal after the third postoperative day Consciousness and rationality returned while the patient was on the operating table There were no more twitchings of the left arm, and he was able to use his arms and legs

normally. He left the hospital on the twelfth postoperative day, a little weak, but otherwise well. He returned to the follow-up clinic five weeks later, he had no complaints and nothing abnormal was found. He was working and living his normal life.

This is a typical case of chronic subdural hematoma: the history and the observations before and at operation, as well as the convalescence. It is interesting to note, however, that because of the large amount of the proprietary drug ingested, a provisional diagnosis of "drug poisoning" had been made. The right-sided flaccidity could easily have been interpreted as a paralytic lesion of the left side of the cerebrum. This case bears out the wisdom of Putnam's suggestion of exploratory punctures.

Alcohol may well have been the predisposing cause, but this, aside from trauma, the inciting cause, was the only one present of the many factors mentioned by Bowen.<sup>5</sup> Calcium deposits have been mentioned by others. Its concentration was insufficient to show in the roentgenograms.

*CASE 2—Subdural hematoma, chronic, onset of symptoms nine days after trauma, psychosis, coma, right subtemporal decompression, removal of clot, recovery*

R. I., a white woman, aged 50, entered the hospital on March 22, 1929, directly after having been struck by a car. The patient walked but complained mostly of pain in the lumbar region.

The results of a general physical examination at this time were essentially negative except for the blood pressure, 190 systolic and 110 diastolic, tenderness elicited over the lumbar spine, and a hematoma in the occipital region.

The results of the neurologic examination were negative. The spinal fluid was clear and under normal pressure.

A headache of three days' duration and some general weakness were the main factors during the next seven days. At this time the headache reappeared. There were a weakness of the right facial nerve (supranuclear) and ptosis of the right eyelid with diplopia of a transient nature. The optic fundi were normal.

The deep reflexes were hyperactive on the right side. The patient became irrational and gradually more drowsy, until at the time of operation she was in a state of coma. In the meantime, the spinal fluid had become xanthochromic, one pressure reaching 200 mm of spinal fluid. The leukocytes rose to 10,050. The urine remained normal. Roentgenograms did not reveal a fracture of the skull. The chemical analysis of the blood gave negative results.

A diagnosis of "chronic subdural hematoma" was made, and moderate right subtemporal decompression was performed. Pulsations were absent. The dura was of a greenish-brown hue, it was opened, and a partially organized clot was exposed. In the center was a brownish-red liquid. The tumor covered practically the entire hemisphere. By means of a brain spoon, liberal quantities of physiologic solution of sodium chloride, cotton pledgets and suction, it was entirely removed. The thicker, central mass was removed in large pieces. The

usual smooth membrane covered the clot and was not adherent to the arachnoid. The brain was compressed, but soon pulsated.

The patient rallied on the table. The field was left dry. The dura, as well as the rest of the wound, was closed tightly.

Section showed a fibrous layer immediately attached to the dura. (A portion of the dura was not removed.) Endothelial leukocytes and red blood corpuscles were found in the interspaces. The capillaries were numerous. A number of large, irregular, endothelial-lined spaces containing red blood corpuscles were arranged side by side with only a small fibrous tissue strand interposed between them and the under surface of the dura. Only a few capillaries and fibroblasts extended into the clot proper. The inner surface of the clot was covered with a thin layer of fibrous tissue and a single external endothelial layer.

On the third postoperative day, the patient complained of general bodily pain and headaches. From then on she improved steadily, and was able to sit up on the fifth day. She left the hospital on the twelfth day in good condition. She was seen three months after discharge, and no residual signs or symptoms were found.

In this case the patient had no complaints referable to the head on entrance; however, within seven days a clear picture of subdural hematoma had presented itself. It was possible to follow the case through its entire course, because relatives refused earlier operative intervention. The patient gave a history negative for alcoholism.

#### SUMMARY AND CONCLUSIONS

1 Chronic subdural hematomas occur more frequently than is generally realized. From the second to the seventh decade, the rate of incidence remained about the same for each ten year period. Several cases have been reported in infants.

2 Trauma is accepted as the determining factor. It is usually of such slight degree as to cause little immediate change.

3 The most important and the most constant clinical observations are latent period, lucid interval, headaches, mental changes, drowsiness, motor disturbances, change in reflexes, disturbances of the cranial nerve, remission of symptoms and coma. The mean average occurrence of these factors is 67 per cent.

4 A group of minor factors is vomiting, nystagmus, sensory disturbance, variation in temperature, pulse and respiration, abnormal fundi, xanthochromic spinal fluid and leukocytosis. The mean average occurrence of these factors is 19.7 per cent.

5 The hematoma is not completely organized, is attached to the dura and is enveloped by a membrane composed of fibrous tissue with a mesothelial covering. Clot occurred on the side of the injury in 80 per cent of the cases.

6 Operative treatment gives the best results. 83 per cent of the patients on whom operations were performed recovered.

7 Complete removal of the clot through the osteoplastic flap is the operation of choice, if the condition of the patient will permit, and accompanying decompression is of value

8 Bilateral burr holes and subdural exploration are advisable in all cases, and would seem preferable to ventriculograms

9 Dextrose, from 50 to 60 per cent given intravenously, and spinal punctures are usually sufficient to take care of the postoperative congestion and edema

10 Drains are seldom necessary in these cases

# TUMORS OF THE GIANT CELL GROUP

A PATHOLOGIC ENTITY \*

C F GESCHICKTER, M D †

AND

M M COPELAND, M D †

BALTIMORE

An outstanding characteristic of all neoplasms is their tendency to reproduce to a limited extent the design and function of the parent tissue, emphasizing the importance of histogenesis in the interpretation of their pathology. In tumors of the giant cell group attention on the pathologic side has been directed usually to only the histologic appearances of these lesions, and because of this shortcoming, much confusion has arisen in classifying these growths, the microscopic resemblance of some of these tumors to granulation tissue having led to a seemingly endless debate regarding their inflammatory or neoplastic nature. In the studies summarized in this article, attention has been directed to the histogenic rather than to the histologic aspects of these lesions, and by an analysis which traces the origin of these tumors to embryonic functions, a fundamental pathologic relationship has been established between various forms of giant cell tumors heretofore considered under separate headings and as individual entities.

In the following pages, a pathologic relationship between the clinical entities of the bone cyst, the giant cell tumor in the long bones and the skull, the epulis of the alveolar border and giant cell tumor of the xanthoma group found in the tendon sheaths is unfolded. The conclusions presented are from an analysis of over 400 cases, supported by data in regard to the age incidence, location, histologic course and embryologic relationship of these tumors which are presented in this paper.

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Submitted for publication, June 12, 1929

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1 For a detailed tabulation of these cases see Geschickter, M M. Osteitis Fibrosa and Giant Cell Tumor, Arch Surg, 112, 1929.

## THE BONE CYST

Although the limits of osteitis fibrosa have been widely extended since the time of von Recklinghausen<sup>2</sup> to include a multiplicity of entities, the solitary bone cyst which is a form of osteitis fibrosa found usually in the shaft of the long bones of young adults presents certain uniform characteristics which throw much light on the nature of the pathologic process involved

Foremost among these characteristics are the clinical features of the age incidence and location of these tumors. In 205 cases of osteitis fibrosa, these expanded and cystic areas of central bone destruction are found, in more than 80 per cent of the cases, to occur in patients under 21 years of age. Furthermore more than 80 per cent of these lesions are situated in the upper end of three long bones in the region of the metaphysis. These predominant sites are the upper end of the femur, the upper end of the humerus and the upper end of the tibia. In the femur they are in the region of the greater trochanter, in the humerus they are in the region of the greater tuberosity, and in the tibia they are in the region of the tuberosity near the epiphyseal line. The roentgenograms illustrate this point. They show an area of bone destruction in a central location near one end of a long bone, overlaid by a cystic expansion of intact thin cortical bone. At the point in the shaft of the bone thus weakened, a pathologic fracture frequently occurs and with the exception of swelling, such a fracture is the most frequent symptom of onset. Clinical follow-ups show that these lesions are always benign and tend to heal after fracture. The average duration of symptoms is two and a half years, and no patient has ever died from the direct cause of the disease.

The occurrence of these lesions in young patients and near the epiphyseal line leads naturally to the conclusion that they are associated with an area of new bone formation, for we know that ossification is not complete in these regions in which bone cysts are most frequent at the time of life at which they occur.

When these lesions are examined pathologically however we are confronted with unexpected results. Instead of the area of newly formed bone proceeding from cartilage which we would expect to find in this metaphyseal location and at this age, an evacuated cavity, generally partially filled with serous fluid is found. There is no remnant left in many cases of bone newly formed from cartilage but instead there is a shell surrounding the cavity, of fibrous tissue overlaid by new bone formation of a different character. The fibrous tissue is rich in

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<sup>2</sup> Von Recklinghausen. Die Fibrose oder deformierende Ostitis die Osteomalacie und die osteoplastische Carcinose, Festschr. z. Rudolf Virchow, 1891

intercellular material, and at many points the fibroblasts are being transformed into osteoblasts which are laying down new bone directly and not via the cartilaginous route. Our studies of this tissue lead to the conclusion that this tissue of fibroblasts and new bone is not an inflammatory reaction as is currently believed, but an extension of the function of the subperiosteal type of new bone formation and represents a healing reaction.

This conclusion is borne out by the work of Macewen,<sup>3</sup> who in his experiments on the growth of bone inside of glass tubes produced a type of ossification from fibrous tissue identical with the areas of new bone seen in sections of osteitis fibrosa (fig 4 B, *Arch Surg* 19.185 [Aug] 1929). The microscopic appearance of the tissue which shows essentially a proliferation of young fibroblasts and osteoblasts resembles more a repair process than inflammation. This repair process is nonspecific and occurs in bone about many different types of bone destroying lesions. It occurs not only in the wall of a bone cyst but also about foreign bodies in the bone, abscesses in the medullary cavity, giant cell tumors, secondary metastatic tumors of the bone and even about primary bone sarcoma.

Pathologically, therefore, osteitis fibrosa is not an entity but a healing reaction around an area of bone destruction. The solitary bone cyst under discussion shows such an area of bone destruction in the form of an enclosed cavity, and about it is the typical healing reaction which we believe is best termed fibrosthosis (indicating new bone formed directly from fibroblasts). Clinically and pathologically, it would seem that the bone destructive process often progresses without noteworthy symptoms, for when we recognize the condition clinically, and make the diagnosis or explore, the bone destructive phase is practically always complete and nothing is encountered but the healing phase. This fibroid process of repair sometimes extends over a period as long as forty-five years and then a latent bone cyst is recognized. The persistence of this healing reaction is due to nature's difficulty in collapsing a cavity with rigid walls and when fracture or a crushing procedure at operation aids in collapsing this cavity, the lesion heals.

*Histologic Variants of the Bone Cyst*—The question arises as to what is the original bone destructive process in the bone cyst. In the average case the lesion is of about two and one-half years' duration when first observed, and at the end of such a period the process responsible for the area of bone destruction has disappeared. When bone cysts are grouped according to the duration of symptoms however and the group

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3 Macewen, W. The Growth of Bone, Glasgow: James Macelhose and Sons, 1912.



in which the symptoms average six months are examined, we are able to discover by pathologic examination the nature of the process which forms this cavity in the bone. The x-ray picture in this group of early cases shows a metaphyseal location and a polycystic structure. Forty-six cases of the series of 205 bone cysts were in this group. Microscopically, they were all classed as giant cell variants of osteitis fibrosa. By this is meant that areas of large multinucleated giant cells embedded in a stroma of round cells (tissue typical of a giant cell tumor) were always found in early cases of bone cyst examined pathologically.

In other words, we are inclined to the belief that the bone destructive phase of osteitis fibrosa is characterized by typical giant cell tumor tissue. More broadly stated, the average solitary bone cyst in the long bones is a healed or healing giant cell tumor. Not only do forty-six early cases of 205 cases of osteitis fibrosa show marked giant cell areas, but sixty cases of giant cell tumor of a series of 226 cases show a healing change toward osteitis fibrosa, most marked at the margins of the tumor, but also infiltrating toward the center.

This does not mean that all bone cysts are healed giant cell tumors, nor is it true by any means that giant cell tumors will all progress toward a healed state of osteitis fibrosa. In bone cysts 2 per cent of the cases can be shown to have a bone destructive phase due to a foreign body or an abscess, and in about 20 per cent of the cases rather loosely classed as osteitis fibrosa, some primary disease, such as osteomalacia, Paget's osteitis deformans, fragilitas ossium or osteo-arthritis is responsible for this cyst formation. The majority of solitary bone cysts (78 per cent), however, show their relationship to a preceding giant cell tumor phase by the persistence of giant cell areas which are most frequent in the younger cysts with a shorter duration of symptoms. This is particularly true of so-called polycystic osteitis fibrosa, which in addition to many areas of giant cells indicates the origin of the large solitary cyst by demonstrating the mode of fusion of smaller cavities embedded in giant cell tissue. This relationship is also evidenced by the fact that the bone cyst arises on the metaphyseal side of the epiphyseal line, bordering on the epiphysis where all giant cell tumors occur, and by the fact that the typical giant cell tumor in the epiphysis shows the same healing reaction of fibro-ostosis or osteitis fibrosa at its margin, although to a less marked degree.

The next question to arise is why the giant cell tumor in the epiphysis fails to heal and is a progressive lesion, whereas the bone cyst which arises close to the same region presents a predominately healing reaction. The explanation lies in the difference between the anatomic structure of the epiphysis and the metaphysis. Both have areas of new bone formation derived from cartilage, and both exhibit a bone destructive tumor characterized by giant cell areas. But the epiphysis lacks the defensive

mechanism represented by the thick cortex of the metaphysis and diaphysis of the long bones, and the overlying periosteum which, as Macewen<sup>3</sup> has pointed out, is equipped in the shaft and the metaphysis with a rich and vascular osteogenic layer, not found in the epiphysis after the age of 3. Hence, the giant cell tumor progresses in the epiphysis, whereas this bone destructive lesion on the shaft side of the epiphyseal line is reacted to effectively by the cortical bone of the metaphysis and as the bone grows, the tumor area is pushed toward the region of the midshaft within the protective confines of the thick cortical bone as a walled-off cavity.

#### NATURE OF THE GIANT CELL TUMOR

The conclusion that the usual bone cyst is an arrested giant cell tumor carries us into the study of the nature of the giant cell tumor in a quest for the origin and etiology of this lesion. The typical giant cell tumor shows an area of bone destruction occurring in the epiphysis of a long bone, and overlying this area there is a thin shell of bone which in many instances is perforated. In our series of 226 cases the average age of the patient is about a decade beyond the average age for the bone cyst. The lesion may occur at any age, but most frequently the patient is in the decade of life between the twentieth and thirtieth years. The age incidence of giant cell tumor when contrasted with that of osteitis fibrosa emphasizes that the difference between these lesions is essentially a difference in the degree of healing, rather than in pathologic nature. The age curves of these growths (fig 31, *Arch Surg* 19:220 [Aug.] 1929) show that as the healing power of the bone cell declines with the advance in the age of the patient, bone cysts decrease in frequency while giant cell tumors increase.

The uniformity with which the giant cell tumor occurs in the epiphysis, and the fact that new bone formation occurs here until late in life leads to the conclusion that the pathologic process involved is associated with the formation of new bone from cartilage taking place in this region. Pathologic examination of these lesions confirms this conclusion, for microscopically cellular elements characteristic of a phase in the ossification of cartilage are found.

The tissue of giant cell tumor is rich in giant cells which contain from 15 to 300 nuclei. These large cells are embedded in a cellular stroma containing many round cells the nuclei of which resemble the nuclei of the giant cell. In the cellular stroma occasional spindle cells are found and also small blood vessels and frequently fresh hemorrhage. The round cells of the stroma seem to be related to the giant cells. The spindle cells are related to areas of osteitis fibrosa and the hemorrhagic areas to strands of newly formed capillaries.

The vascular and cellular stroma seen in giant cell tumor resembles the tissue seen when the marrow cavity is being formed in the embryo. The giant cells that predominate the microscopic picture resemble the large osteoclasts which are associated with the resorption of calcified cartilage that takes place in the histogenesis of bone derived from cartilage. Embryologic studies carried out to determine this point have led to the conclusion that the giant cell tissue observed in giant cell tumors corresponds in nature and structure with a normal phase in the substitution of calcified cartilage by permanent bone.

*The Rôle of the Giant Cell in the Histogenesis of Bone*—In the embryo, the long bones are preformed in cartilage, and ossification begins in the center of the shaft and works its way toward the epiphysis, leaving the metaphysis and the epiphysis (the latter with a separate center of ossification) to be ossified in later life. The cartilage cells initiate the bone formation by laying down an increased matrix which becomes calcified, they then atrophy within the small calcified chambers known as the primary areolae. The giant cells appear on the scene after this temporary calcified structure has been laid down. They travel inwardly toward the calcified shaft from the primitive periosteum and penetrate the small rim of subperiosteal osteoid tissue to gain entrance to the central calcified area. In their wake they carry new blood vessels and primitive osteoblasts, and once inside of the calcified central area, destroy it, creating the medullary cavity.

This penetrating rôle of the giant cell, in the embryo, which provides for vascularization and the resorption of temporary bone, we believe is duplicated in giant cell tumor.

*Giant Cell Tumors of the Skull*—If the view is correct that the giant cell tumor preserves its embryonic bone-destroying functions, and this tumor is fundamentally related to the proliferation of osteoclasts in bone newly formed from cartilage, then a study of giant cell tumors of the head should furnish valuable evidence in confirmation of this view. For we know that a large part of the bones of the skull and face are formed from membrane, and therefore, the typical giant cell tumors that occur in the head should not arise in these bones, but only in those derived from cartilage. Twenty-two giant cell tumors of the head were examined in an endeavor to prove or disprove the relation of giant cell tumors to cartilaginous bone. Briefly, the results were as follows. Two of the lesions were found in the temporal fossa, fourteen were found in the lower jaw, and six were found in the upper jaw or maxilla. A study of the clinical history and x-ray pictures showed that the two lesions in the temporal fossa arose from those portions of the sphenoid bone derived from cartilage. The fourteen lesions of the mandible could be accurately located in twelve cases.

Nine of these were in the region between the symphysis and mental foramen, just at that point where Meckel's cartilage aids in the formation of the lower jaw, and the other three lesions were in the ramus at the site of another cartilaginous center of ossification. Some difficulty was encountered in establishing the origin of central giant cell tumors of the upper jaw. The maxilla is formed from membrane, but the six lesions in this bone showed a unique tendency to present always into the antrum or the orbit, and when carefully traced, it was found that the ethmoid bone, which is formed from cartilage, and which borders on both the antrum and the orbit, was responsible for the origin of these tumors.

*Epulis*—A study of giant cell tumors of the head has confirmed the view that these tumors are related to the process of new bone formation proceeding via cartilage. Another form of giant cell tumor which occurs on the alveolar border of the upper and lower jaws must now be considered from this standpoint. The lesions in this locality have been known for centuries under the name of epulis, and this appellation which means "upon the gums" has been responsible for the inclusion of a multitude of miscellaneous and extraneous entities under this category. When a careful analysis is made, it is possible to split off from this collection a clinical entity composed of a giant cell and a fibroid type of epulis. Histologically, the giant cell epulis resembles the giant cell tumor, and the fibroid epulis resembles osteitis fibrosa, once more illustrating the relationship of these two lesions, the one a destructive phase, the other a predominantly healing reaction. It is to be inferred, therefore, that the epulides are homologous lesions to the giant cell tumor and the bone cyst, and we must explain how these lesions arise independently of a cartilaginous center of ossification. For Bloodgood<sup>4</sup> has shown that these tumors are derived from the alveolar dental periosteum, and this periosteum along the borders of the upper and lower jaws rests on membranous bone and not on bone derived from cartilage. Apparently, these lesions constitute an exception to the general rule just formulated, but the matter must be considered in more detail.

Clinically, the type of epulis under consideration occurs in young people, mostly between the ages of 6 and 30. In our series of cases, we have never found this type of epulis in a patient under 5½ years, nor in a patient over 43 years. Another unique observation in our series of cases (and borne out by 178 cases collected by Scudder<sup>5</sup>) was the fact that the typical epulis rarely occurs at the site of the last molars. Once again the age incidence and location of the lesion give

4 Bloodgood J. C. Epulis. *Am Pract Surg* 6:818, 1909.

5 Scudder, C. L. *Tumors of the Jaw*, Philadelphia W. B. Saunders Company, 1912.

the clue to the pathology. These molar teeth, where the epulis does not arise, are permanent and not deciduous teeth, and the age limit on the lower side in which children under 5 are shown not to be subject to epulis, is the period before the shedding of the deciduous teeth. We come to the conclusion, therefore, that the epulides arise in the process of shedding the deciduous teeth. It is interesting and more than suggestive that these deciduous teeth are temporary bony structures just as calcified cartilage in the epiphysis and the metaphysis of the long bones and in the chondiocranium of the skull is a temporary bony structure. The epulis, therefore, is thus related to the process of the resorption of the temporary bony structure of the deciduous teeth. It now remains to be demonstrated whether the giant cells here as elsewhere are osteoclasts active as agents in the resorption of the temporary bone. Histologic studies of the roots of the deciduous teeth at the ages that the milk teeth are being shed show this to be the fact. At this time there is a proliferation of giant cells (in this case odontoclasts) which arise from the periosteum and attack the cementum of the roots of the deciduous teeth and loosen them, preparing the way for the eruption of the permanent teeth.

*Giant Cell Tumors of the Xanthoma Group*—Giant cell tumors of tendon sheaths which have been traditionally classed with the so-called xanthoma are with difficulty brought into line with the conception entertained here of the relationship of temporary bone resorption to giant cell tumor.

Fortunately, the records of two giant cell tumors of the patella demonstrated that a sesamoid bone embedded in a tendon may give rise to this type of lesion in soft part structures. A study of other sesamoid bones shows that these small bones, which are derived from cartilage are situated most frequently at the metacarpophalangeal joints of the hands just where giant cell tumors of the tendon sheaths are most commonly found. This coincidence suggests these bones as a source of origin for so-called giant cell tumors of the tendon sheaths, and this is corroborated by histologic studies.

When giant cell tumors of the tendon sheaths are examined microscopically, a variant of the typical giant cell structure is seen, characterized by an unusual amount of pink staining fibroid tissue, enclosing in a network cells of the cartilage type. This fibroid substance on further investigation is identified as the vestige of white fibrocartilage from which the sesamoid bones are derived.

Thus giant cell tumors of the tendon sheaths which have long been erroneously classed under the heading of xanthoma, are in reality tumors of the sesamoid bones. By removing these tumors from the confusion of the so-called xanthomatous lesions, the current "granu-

lation tissue" conception of them is overthrown, and their giant cell structure is related to the resorption of cartilaginous bone. This brings these tumors into line with the conception of giant cell tumor advanced throughout this paper.

*Etiology of the Giant Cell Tumor*—It is much easier to discuss the etiology of tumor in terms of so-called etiologic factors than to point out the initial event and a subsequent unbroken chain of histologic consequences. For this reason, the literature abounds with references to the etiologic factors of trauma and hemorrhage in the production of giant cell tumor and bone cysts. Konjetzny,<sup>6</sup> Lubarsch,<sup>7</sup> and Pommer<sup>8</sup> are among those of the German school that have attempted to trace the bone cysts to medullary hemorrhage following trauma. We are in accord with these authors in placing trauma in a primary position in the production of these lesions. An attempt will be made, however, on the ground of the embryologic observations pointed out earlier, to show just how trauma acts histologically in producing the bone cysts and the giant cell tumor.

In our series of 226 cases of giant cell tumor and in others in the literature, trauma was obtained in the history of the patient in between 40 and 50 per cent of the cases. Assuming that in the major portion of the other 50 per cent of the cases there was an overlooked and insignificant trauma, it can be pointed out how the prevalent sites for the lesions of giant cell tumor and bone cysts are related to such injury.

The three main locations of bone cysts are in the metaphysis of the femur in the region of the greater trochanter in the humerus at the site of the greater tuberosity and in the tibia at the tuberosity. These sites at the hip and at the shoulder receive the brunt of the trauma. The epiphysis in the head of the femur and the head of the humerus are shielded by the acetabulum and the glenoid cavity and hence escape frequent injury. This is why a bone cyst and not a giant cell tumor arises here for it is the metaphysis and not the epiphysis that is traumatized and as we have seen, this difference between a metaphyseal and an epiphyseal location constitutes the real distinction between a bone cyst and a giant cell tumor. At the lower end of the radius and at the lower end of the femur on the other hand it is the epiphysis which is exposed and as a consequence the giant cell tumor is the resultant lesion rather than a cyst. In the head of the tibia

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6 Konjetzny G E Die sogenannte "lokalisierte Ostitis fibrosa," Arch f klin Chir **121** 567 1922

7 Lubarsch Die Bedeutung des Traumas zur Entstehung und Wachstum krankhafter Gewächse, Med Klin **41** 1651, 1912

8 Pommer G Zur Kenntnis der progressiven Hämatom und Phlegmasie-veränderungen Arch f Orthop u Unfall Chir **17** 17 1919

both the epiphysis and the metaphysis share alike in exposure to injury, and at this site, both types of lesions are common

Close examination of these sites which so frequently harbor the lesions under discussion, discloses certain interesting details in regard to the initial form of these growths. In an early giant cell tumor (from two to six months' duration instead of the average of fourteen months) the original seat of the lesion is usually asymmetrical in location and subcortically located at one side of the epiphysis (fig 59, *Arch Surg* 19:266 [Aug] 1929). As the lesion progresses, it extends centrally rather than peripherally, because the cortex is more resistant than the medullary cancellous bone, thus obscuring the early typical subcortical location. When we examine the early bone cysts in the metaphysis of from five to six months' duration, instead of the average duration of two and one-half years, we find that this lesion also has a subcortical location. In other words, both the bone cyst and the giant cell tumor arises at a point just beneath the traumatized area of the cortex.

Referring to the work of Lexer<sup>9</sup> on the blood supply of the bones (fig 58, *Arch Surg* 19:265 [Aug] 1929), it is seen that both the epiphysis and the metaphysis receive their blood supply from anastomoses around the joints which send in arterial branches that penetrate the cortex more or less at right angles, proceeding inwardly after the fashion of the periosteal blood supply in the shaft rather than by a central medullary course, as is characteristic of the nutrient artery. The effect of trauma on the blood supply here is to cut off the arteries proceeding inwardly from a cortical position at the epiphysis or metaphysis producing a subperiosteal hematoma. This interruption deprives the cortical bone in these regions of its nourishment and creates a need for collateral circulation by a medullary route. The result is an increased proliferation of the osteoclasts in the medullary cavity in order to open up channels for the budding capillaries proceeding outward toward the injured area. As we have seen, this is a normal histogenic function of the osteoclasts. But this increased osteoclastic activity in an area in which they are already unusually active in the rôle of new bone construction, occurs just at that time when unnourished cortical bone is undergoing necrosis. An imbalance is thus created between bone destruction by osteoclasts and new bone formation that would normally proceed from the reactive cortex were its circulation intact. The defensive reaction of cortical bone, therefore, is suspended while bone destruction by osteoclasts is at its height. This imbalance results in an unchecked hyperplasia of the osteoclasts and produces a tissue

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<sup>9</sup> Lexer, E. Die Entstehung entzündlicher Knochenherde, *Arch f klin Chir* 71 1, 1903

characteristic of giant cell tumor and the early phase of osteitis fibrosa or bone cysts

In the metaphysis the reactive cortical bone which is thick and vascular, is apparently capable after a time of overtaking the osteoclasts. In the epiphysis however, bone destruction seems to proceed at a faster rate than the thin cortical bone in this region can overtake. The result is an arrested lesion or bone cyst in the metaphysis and a progressive or unchecked lesion in the epiphysis which is known as the giant cell tumor. Even in the epiphysis, however the balance can be restored if surgical intervention is made before the bone shell is too extensively destroyed. By removing the osteoclastic tissue by the curet and cautery (and we suggest by aiding nature to collapse the bone cavity remaining) the giant cell tumor will also go on to ultimate healing.

That additional metabolic factors may enter into the production of this imbalance between bone destruction by the proliferation of giant cell osteoclasts, and the formation of reactive cortical bone by a process of fibro-ostosis, is shown by studies made on multiple giant cell tumors and multiple bone cysts. In a series of twenty-one cases analyzed in this group it was found that the patients were either women past the age of puberty in the osteomalacia period or boys or girls in the age of juvenile bone diseases. The case studies showed that osteomalacia, syphilis, rickets, fragilitas ossium and other associated skeletal diseases were frequently present and were contributing factors in the production of these lesions and their extension to several bones. More recently, at the Mayo Clinic Dr. R. M. Wilder (in a case to be reported in *Endocrinology*) has placed at our disposal evidence indicating that disturbances in the calcium and phosphorus metabolism associated with hyperparathyroidism due to an adenoma in the parathyroid glands, may favor the production of multiple giant cell tumors in a female past the age of puberty. We ourselves have confirmed this by observing similar disturbances in the calcium metabolism in a patient with a solitary giant cell tumor of the lower part of the radius arising during the latter half of pregnancy.

Thus histologically trauma is related to the bone cysts and the giant cell tumor not as an indefinite etiologic factor but as an initial event in disrupting the cortical blood supply which produces an imbalance between osteoclastic proliferation in the medulla and reactive compact bone in the cortex. In the etiology of these lesions individual variations in collateral circulation as well as the extent of the injury to the cortical bone are important factors. Disturbances in the calcium and phosphorus metabolism must also be considered in the oncology of these growths. It is evident however from the study summarized



here that the age of the patient, the site of the injury, the rate and extent of cartilaginous ossification at the end of the bone and the nature of the blood supply in the affected region are the predominant factors in the pathology of bone cysts and giant cell tumors

When all these factors are considered, it is apparent why both bone cysts and giant cell tumors are rare in comparison to the frequency of trauma. It must be emphasized that to have the lesions clinically an imbalance in two normal repair processes is necessary—an unusual increase of osteoclastic proliferation and a diminution or suspension of new bone formation in an injured cortex. These two processes are always active after injury to bone (fig 57, *Arch Surg* 19:263 [Aug] 1929). Both fibro-osteosis (osteitis fibrosa tissue) and osteoclastic proliferation (giant cell tumor tissue) are to be seen after ordinary fractures and in the healing of a subperiosteal hematoma (Cone<sup>10</sup>). Only when the bone destructive phase of giant cell proliferation is in the ascendancy for a significant period do the clinical entities of giant cell tumor or osteitis fibrosa arise. The factors concerned in the ascendancy of such giant cell proliferation we may list (by way of summary) in the order of their importance as: 1. A normal histogenic proliferation of giant cells which occurs only in calcified cartilage or the temporary bone of the roots of deciduous teeth. 2. Injury and necrosis of an area of cortical bone overlying an actively ossifying epiphyseal or metaphyseal region. 3. A response on the part of giant cells and capillaries in cancellous bone to the need for collateral circulation. 4. Disturbances in the calcium and phosphorus metabolism inhibiting the normal growth and defensive reaction of cortical bone.

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10. Cone, S. Ossifying Hematoma, *J Bone & Joint Surg* 10:474, 1928

# FETUS RETENTION FOR TWENTY-SIX MONTHS

## REPORT OF A CASE \*

HARTMAN A LICHTWARDT, M D

MESHED, PERSIA

This case is interesting for three reasons (1) the length of time the bones of the fetus were retained in the uterus, (2) the formation of fistulas between the transverse colon and the fundus, and (3) the method of repair

### REPORT OF CASE

*History*—A Kurdish woman, aged 30, was admitted to the temporary field hospital of the American Presbyterian Hospital of Meshed, in Kuchan, Persia, Sept 29, 1928, on account of a tumor of the abdomen. The patient had been married fifteen years, and had had five children, all of whom had died before the age of 3 (not an unusual happening in Persia). Eight years previously, in her fourth pregnancy, she had a miscarriage at four months. There was no history of venereal disease.

In July, 1926, the patient, then eight months pregnant, with a moving fetus, was frightened by an aeroplane which was dropping bombs near her village, and she stumbled and fell as she ran into the house. There was no immediate pain, but the fetal movements ceased, and three weeks later the woman was uncomfortable, with aching pains, which never resembled labor pains. She had occasional periods of fever, with a foul discharge after the sixth week, which grew more copious. Two months after the cessation of fetal movements, several small pieces of bone were observed in the discharge, and during the following year, she noted pieces of fetal bones in the discharge on several occasions. The bones of the feet and legs were recognized.

This woman had no medical treatment of any kind. Part of the time, she was up and around, doing some of her primitive housework, and part of the time, lying down, depending on the amount of fever and discomfort. Near the end of June, 1928, a small fistula opened in the abdominal wall, 15 cm to the right of the umbilicus. As soon as this developed, the pain in the middle part of the abdomen, which had become rather severe, grew less, the vaginal discharge ceased, and a considerable amount of foul-smelling fluid was discharged from the fistula. A week later, the patient noted some feces and grape seeds passing out of this opening. No fecal matter ever passed out of the vagina, nor had the patient menstruated since the beginning of this last pregnancy. There had been occasional vomiting but no evidence of intestinal obstruction at any time.

*Physical Examination*—The patient walked bent over, owing to abdominal discomfort. She was thin, pale and emaciated, with a temperature of 98.3 F, and a pulse rate of 120 weak but regular. There was a hard tumor of the abdomen, the size of a grapefruit, the top of which was 3 cm above the umbilicus. The tumor was approximately in the midline extending a little more to the right than to the left. It was firmly attached to the abdominal wall and tender to

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\* Submitted for publication Dec 31 1929

\* From the American Presbyterian Hospital

touch One and one-half centimeters to the right of the umbilicus, there was a fecal fistula, nearly 0.5 cm in diameter, with some irritation of the surrounding skin, due to the constant foul discharge Vaginal examination showed the cervix to be slightly larger than normal, containing scars of previous lacerations, there was some dilatation, but no discharge The uterus was not movable, and bimanual examination showed that from the cervix to the top of the tumor, all was one mass

*First Operation*—With the patient under ether anesthesia, a right rectus incision was made, extending from the level of the umbilicus to 6 cm below An opening was made directly into the uterus, without opening the peritoneum The contents of the uterus were then removed and consisted of all of the bones of the fetus, except those of the feet and legs, all in a good state of preservation and lying free in the uterus Some feces and some grape skins and seeds were also removed, there was no evidence of placenta or membranes In the posterior wall of the uterus at the level of the umbilicus, and 7 cm to the right of it, was an opening into the transverse colon, near the hepatic flexure Fecal matter entered the fundus freely through this opening On the left posterior wall of the uterus, just below the level of the umbilicus, and 6 cm to the left of it, there was a second opening into the transverse colon, near the splenic flexure A saline enema was given and at once appeared through the opening, indicating its nearness to the rectum There was no connection between these two openings in the transverse colon, except through the uterus

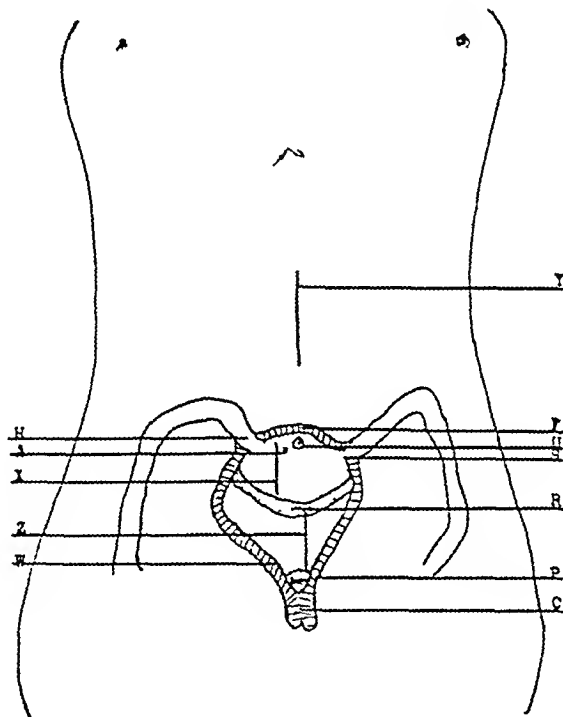
A large catheter was passed from above downward, through the cervix into the vagina, to provide drainage of the uterus from below A second catheter was inserted into the opening into the splenic flexure, so that the rectum could be washed out from above A larger tube was inserted into the hepatic flexure so that this colostomy might drain outside The incision was then sutured around these tubes, the original fistula of the abdominal wall having been first excised The patient rallied quickly from this brief operation, the only rise of temperature being that to 101.1 F on the day following

*Second Operation*—As my stay in Kuchan was to be but a few weeks, I operated on the patient again five days later (Oct 3, 1928) under procaine hydrochloride infiltration anesthesia, a midline incision being made extending upward for 10 cm, from a point 4 cm, above the umbilicus I hoped to make an anastomosis between the two ends of the transverse colon and do a complete hysterectomy, but on opening the abdomen, I found that the colon, the uterus and the adnexa were all so firmly bound together by old adhesions that such an anastomosis was impossible This upper abdominal wound was sutured without drainage, there was no elevation of temperature or acceleration of pulse after this exploratory operation

*Third Operation*—The patient being anxious to be cured before the temporary field hospital was closed, I operated again one week later, using procaine hydrochloride infiltration anesthesia, and making a midline incision extending downward for 10 cm from a point 8 cm below the umbilicus The peritoneum was opened below the point at which the fundus was adherent to the abdominal wall Previous to this the vagina had been thoroughly cleansed and the cervix swabbed with tincture of iodine, while the drainage tubes had been removed, and long tape sponges inserted into the two openings of the transverse colon, and the entire fundus swabbed with tincture of iodine A partial hysterectomy was done, just above the internal os, which was firmly sutured The fundus was then sutured from below, and the peritoneum closed without drainage The great amount of adhesions between the uterus and adnexa and the colon made it impossible to do

an anastomosis of the colon from below. Through the open incision of the first operation, where drainage tubes had been inserted, the gauze plugs were removed and this original opening of the abdominal wall was tightly sutured in the faint hope that it might possibly heal by first intention even though a steady fecal flow would be passing through this fundus, which had now been converted into part of the intestinal tract. Both the upper and the lower midline incisions healed, but a small fecal fistula developed in the right rectus incision after a few days. The patient had a slight rise of temperature (101.2 F) on the third day of the operation, except for that, her condition was good.

*Course*—Two weeks after this last operation the field hospital had to be closed and a return made to Meshed, at this time the patient's temperature, pulse and respiration were normal and she was sitting up in bed eating well and not



A drawing showing the size and the position of the uterus, the site of the three operations and the method of repair. *H*, opening of transverse colon near hepatic flexure, into uterus, *A*, fistula from uterus through anterior abdominal wall, *X*, site of first operation, *Z*, site of third operation, *II*, wall of uterus, *I*, site of second operation, *F*, top of fundus of uterus, *U*, umbilicus, *S*, opening of transverse colon, near splenic flexure into uterus, *R*, after repair showing how fundus was made into part of the colonic passage, *P*, after repair, showing where uterus was amputated above internal os, *C*, cervix.

complaining of pain. The fecal fistula was 0.4 cm in diameter but most of the feces were passing through the rectum in the proper way. There was no vaginal discharge or bleeding, nor was there any blood issuing through the anus.

Instructions were given to the husband, regarding the cleansing and dressing of the fistula, and the care of the patient and a supply of sterile gauze was left with him. The last week in November he came to Meshed and reported to me that there was still a slight watery discharge from the fistula but no

feces, the patient had returned to her village, where she was walking, although still weak. She had no pain or fever, her bowels moved regularly, and her appetite was fair. The husband was given a small bottle of 90 per cent silver nitrate solution, with instructions to apply a little of this caustic daily to the fistula after cleansing it. Toward the end of January, 1929, the husband again came to Meshed and reported that the fistula had entirely closed, and that the patient was well and doing her housework. I had hoped that the woman would come to Meshed that she might be given a barium enema and some roentgen films be secured, but she has not done so yet.

## COMMENT

The history of the woman's fall was sufficient to account for the death of the fetus, but it is more difficult to explain why labor did not start, possibly this was owing to the old scars of the cervix, the result of former lacerations. Both Williams<sup>1</sup> and De Lee<sup>2</sup> mention "missed labors" briefly, and cite the cases of Menzies<sup>3</sup> and Hennig,<sup>4</sup> in which the fetus was retained for 280 and 210 days, respectively, after full term. Many cases are recorded of lithopedions especially in extrauterine pregnancies, one in China<sup>5</sup> retained three and a half years, and several reported by Masson and Simon,<sup>6</sup> who also give an extensive bibliography. Sourasky<sup>7</sup> reported a simultaneous abdominal and tubal pregnancy with retention of the fetuses for two and a half years, but the longest retention of which I can find record is that reported by McCormick,<sup>8</sup> the fetus was retained in the abdomen for fifty years. In practically all of these cases, mummification had set in. Cases with purulent disintegration, however, are rare. Cohen<sup>9</sup> reported one in which the 4 months old fetal head was carried in the uterus four years. In the case which I report, the majority of the bones of an 8 months old fetus were in the uterus for twenty-six months, with ulceration into the transverse colon in two places and a fistula of the abdominal wall finally developing.

One may assume that the fundus soon became adherent to the anterior abdominal wall and remained fixed there, but it is more difficult to visualize the pathologic changes between the posterior wall of the uterus and the transverse colon, with ulcerations due to the pressure of the

1 Williams, J. W. *Obstetrics*, ed 5, New York, D. Appleton & Company, 1926, p 164.

2 De Lee, J. W. *Obstetrics*, Philadelphia, W. B. Saunders Company, 1913 p 474.

3 Menzies. *Glasgow M. J.*, July, 1843, p 229, quoted by De Lee.

4 Hennig. *Arch. f. Gynec.* **13** 292, 1878, quoted by Williams.

5 L. M. S. Margaret Hospital for Women. *China M. J.* **38** 504 (June) 1924.

6 Masson, J. E., and Simon, H. E. *Surg. Gynec. Obst.* **46** 500 (April) 1928.

7 Sourasky, M. *Lancet* **2** 650 (Sept 25) 1926.

8 McCormick, E. J. *Ohio State M. J.* **22** 501 (June 1) 1926.

9 Cohen, H. *M. J. & Rec.* **126** 369 (Sept 21) 1927.

fetal bones As this was taking place and part of the transverse colon was being eliminated, why were there not violent symptoms of obstruction and toxemia?

The question may be raised of the possibility of obstruction if the thick wall of the uterus should undergo involution and reduce the size of the passage It is doubtful whether uterine tissue which has been infected and hypertrophied for such a long time ever regains its tone and becomes contracted The long retention of the fetal skeleton with the constant state of infection of the uterus and the subsequent formation of fistulas indicate the extent to which nature is able to take care of infection, and the unique methods she will use to get rid of foreign materials that cannot be absorbed I believe that if surgical intervention had not occurred at this point, gradually all of the fetal bones would have been discharged through this fistula of the abdominal wall

One might consider whether there is any danger of toxic absorption by the fundus, which is now being used as part of the large colon Probably the months of infection and irritation have so greatly diminished the absorbability of the walls of the uterus that it merely acts as a mechanical passage If menstruation should ever recommence, which is extremely doubtful, the fluid will, of course, be readily discharged through the rectum

#### SUMMARY

The case reported is that of retention of the skeleton of an 8 months old fetus for a period of more than two years, during which two fistulas were formed between the fundus of the uterus and the transverse colon, and finally a fistula between the uterus and the anterior abdominal wall The fetal bones were removed, but it was found necessary to do a partial hysterectomy, and the fundus was used to form the passage between the two openings of the transverse colon

# A REVIEW OF UROLOGIC SURGERY \*

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## KIDNEY

*Surgical Technic*—Halbfas-Ney<sup>1</sup> reviewed data on resection of the twelfth rib in many cases during recent years. Reports of this procedure in the literature are meager, and opinions as to its merits are varied. Israel and Albanian seldom used the procedure, Kuster observed it only once, and Wildbolz used it only twice in 175 cases of renal tuberculosis. Kummell, Frangenheim-Wehner and Israel are of the opinion that incision of the kidney should be extended anteriorly for better exposure. Schmieden resected the twelfth rib twenty-nine times in 92 cases in which nephrectomy was performed, in 1 case the eleventh rib also was taken. The possibility of injuring the pleura has been an objection to this method, but such injury occurred in only 3 cases of Halbfas-Ney's series. He resected the twelfth rib in all cases if the kidneys were high-lying, as well as in those in which the kidney was adherent in the region of the upper pole.

In a series of 203 cases of nephrectomy, the rib was resected in 56 (36 per cent). The surgical indications were tuberculosis in 25 cases (44.6 per cent), tumors in 12 cases (21.4 per cent), pyonephrosis in 15 cases (26.8 per cent), and hydronephrosis in 4 cases (7 per cent).

\* Submitted for publication, April 26, 1930

<sup>1</sup> Halbfas-Ney, P. Die Resektion der letzten Rippe im Dienste der Nierenfreilegung, *Ztschr f urol Chir* **27** 275 (May) 1929

There were also 2 operations of pyelotomy, 1 of nephrostomy, and 2 exposures which were carried out with resection of the rib, making 61 resections. Follow-up records showed that only 46 of the patients were alive. The wounds of these had all healed uneventfully. The region of the resection showed deep retraction. Pain was not felt on deep breathing, and the stump of the resected rib was not painful on pressure. A few patients noted slight anesthesia of the area or a tickling in the scar, as well as light, radiating pain on exertion. Halbfas-Ney expressed the belief that these conditions are due to the paresthesia of the cut nerves and not to resection of the rib.

[ED NOTE—It may be necessary in certain cases to resect or fracture the rib. Halbfas-Ney seems to have used this method more frequently than is the common practice. One of the great advantages of the Mayo incision is its possibility of being carried forward. This, together with the division posteriorly of the lateral arcuate ligament, should give adequate exposure in most cases. Should more exposure posteriorly and superiorly be necessary, simple fracture of the twelfth rib may be employed. Resection of the rib is in itself a major operative procedure and should be reserved for those cases in which other methods of exposure have not been satisfactory.]

Hepburn<sup>2</sup> reported a case in which resection of half of a solitary double kidney was performed. He concluded that partial nephrectomy in such cases can be done successfully with marked compensatory improvement in the function of the remaining portion of the kidney. The simplest and safest method of heminephrectomy of the diseased double kidney is to separate the halves by blunt dissection with the finger. The cleavage will be at the point of least resistance, between the terminals of the blood vessels. This avoids the danger of destroying the circulation to the good portion of the kidney and of cutting into calices. A few pressure mattress sutures to control the oozing of blood are all that is necessary to place in the cut end, and it is not essential to cover the raw end with renal capsule.

Walters<sup>3</sup> considered that the most desirable cases for heminephrectomy are those in which there is complete duplication of the renal pelvis and ureter and in which it is necessary to remove only the

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<sup>2</sup> Hepburn, T. N. Hemiresection of a Solitary Kidney, *Ann Surg* **90** 402 (Sept.) 1929.

<sup>3</sup> Walters, Waltman. Heminephrectomy or Resection of a Part of the Kidney. Report of Four Cases. *Surg Gynec Obst* **50** 473 (Feb.) 1930.



portion of the kidney involved by the lesions. He reported three cases in which successful resection of the diseased portion of a duplicated kidney was carried out, and also one resection of the lower pole of a kidney containing a large solitary cyst. Success of the operation depends on not opening into the adjacent calix of the remaining portion of the kidney and on the assurance of complete hemostasis at the site of the resection. It is an advantage, after beginning the resection to place a finger in the dilated calix and pelvis of the portion to be resected, so as to assist in determining its outer limits. It has not seemed necessary during the resection, even temporarily, to interfere with the blood supply to the remaining portion of the kidney. Immediate bleeding from the cut renal parenchyma stops quickly with the placing and tying of mattress sutures over small bits of muscle tissue and approximation of the cut edges of the kidney. A v-shaped resection, when possible, aids in carrying out this procedure. Pieces of muscle are used to prevent the mattress suture from tearing through the parenchyma.

In three of the cases such excellent approximation was obtained that after the mattress sutures were placed, the edges of the fibrous capsule could be approximated with a running suture. In the case in which this was not possible the denuded area of the kidney was covered with a portion of the perirenal fat in the form of a patch. Studies were made preoperatively and postoperatively of the function of each kidney separately, and pyelograms were made of the duplicated kidney. Resection of the diseased portion of the kidney did not interfere with the function of the remaining portion, and in each instance resection was followed by excellent results.

*Anomalies*—Thompson<sup>4</sup> noted 19 cases of horseshoe kidney in a review of approximately 13,000 reports of necropsies. Sixteen cases occurred in men and only 3 in women. The condition is much more common in men, thus differing from the sex incidence of solitary kidney. The anomaly was recorded at almost all ages, but the average for men was 35 and for women, 24.

Horseshoe kidneys are situated lower than normal kidneys, on planes extending from below the level of the brim of the pelvis as high as the third lumbar vertebra. The union of the two kidneys may be formed by true renal tissue, at either the upper or the lower pole, the latter occurring more frequently. A fibrous tissue bridge is not recorded in

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<sup>4</sup> Thompson, A. R. Horseshoe Kidney. *Guy's Hosp Rep* 79:201 (April) 1929.

these cases Horseshoe kidneys are usually heavier than the weight of two normal kidneys

The ureters passed in front of the mass in 7 cases, and behind the mass in 1 case The ureters were double, except in 2 cases in which they were single Horseshoe kidney is rather uncommon, the incidence was 1 in 700 cases coming to necropsy Renal function was poor in one fourth of the cases One third of the patients died from some infective process

Kretschmer<sup>5</sup> reviewed reports in the literature of 30 cases of true supernumerary kidney, 1 of which was his own It is his belief that this condition is less common than any other congenital renal anomaly Twenty-one of the cases were observed clinically, and 8 were discovered at necropsy The largest number of patients were in the second decade of life, which would seem to justify the conclusion that this renal anomaly tends to produce pathologic changes in the kidney early in life In 17 patients, the left side was affected and in 12, the right, in 1 case the site was not mentioned In most of the cases the site was given rather accurately, that is, below the so-called normal kidney Usually in this type of anomaly only 2 ureteral orifices are found in the bladder, which appears normal in the cystogram

Lesions were present in 19 of the supernumerary kidneys Stone and infection were the most common Stones occurred in 3 cases, in 2 cases they were found not only in the supernumerary kidney but in the other kidney on the same side In another case all 3 kidneys were the seat of stones and severe infection The supernumerary kidney was normal in 7 cases and in 4 cases the condition was not mentioned The other kidney on the side affected was normal in 14 cases, and a lesion was not mentioned in 6 cases, thus a lesion was present in 10 cases only As in the supernumerary kidney, calculus was the most common condition, having been reported in 4 of the 10 cases

Pain was the most constant symptom, being present in 16 cases The description, duration and site of the pain varied, it was described as epigastric, abdominal, renal colic and pain in the left side of the abdomen Palpable abdominal tumor was noted in 14 cases, tumor was not present in 7 cases, and in 9 cases tumor was not mentioned

McCown<sup>6</sup> described renal ectopia as a condition in which the kidney is congenitally in a faulty position and its blood supply is anomalous

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<sup>5</sup> Kretschmer, H L Supernumerary Kidney, Surg Gynec Obst **49** 818 (Dec) 1929

<sup>6</sup> McCown, P E Bilateral Renal Ectopia, J Urol **22** 653 (Dec) 1929

This distinguishes ectopic kidneys from low-lying kidneys with the blood supply coming from the proper level of the aorta. Ectopic kidneys are usually smaller than normal. The pelvis is on the front in the pelvic type of kidney and varies with the ascent and degree of rotation in the high positions. In bilateral ectopia, the kidneys may be fused or lie close together in the pelvis, the left is usually slightly lower than the right. The ureters are normal but short, unless abnormality of the bladder exists. Kidneys of this type are likely to be lobulated, their posterior walls are creased by contact with the rim of the bony pelvis or rounded out to fit into the hollow of the sacrum when wholly within the true pelvis. They lie behind the mesosigmoid or the structure of the vicinity into which they encroach. Ectopic kidneys are vascularized from the proximal vessels in the plane in which they lie, those in the pelvis receiving their veins and arteries usually from the common iliac or the common and external iliac veins, whereas those in the false pelvis are vascularized from the lower part of the aorta and vena cava. The misplaced kidneys may function normally, as in McCown's case for sixty-seven years. The most common lesions are pyelonephritis and hydronephrosis, calculus, sarcoma and tuberculosis have been reported.

The symptoms usually consist of sacro-iliac backache, pain in the lower part of the abdomen radiating frequently to the hips and limbs, and increasing during menstruation.

Pyelitis in ectopic kidney can be cured in about the same ratio as in normally placed kidneys and by the same treatment. In the non-fused cases, nephrectomy may be done, the only difficulty consists in locating and controlling the anomalous blood supply. Pyelotomy may be done in some cases. Nephrotomy is not desirable. Attempts at fixing ectopic kidneys at a higher level have usually failed because of short ureters and the blood supply.

[ED. NOTE.—The care to be used in distinguishing true renal ectopia from simple nephroptosis, as described by McCown, is important. Operative procedures, such as fixation or suspension, undertaken without recognition of the ectopic blood supply and short ureter, may lead to serious difficulty and perhaps disaster. Likewise the treatment of pathologic conditions such as stone or infection in this type of kidney must be approached with conservatism and with a full knowledge of the anatomic peculiarities of such anomalously placed organs.]

Thompson,<sup>7</sup> in reviewing a series of records of necropsies, found 32 cases of solitary kidney, a proportion of 1 solitary kidney to 400 necropsies. This observation reveals that the condition is much more common than some observers have noted. In the necropsy reports from the London Hospital, the proportion was 1 in 124 cases. There were 15 female and 17 male patients. Patients with this anomaly are not good risks for treatment. Excluding children under 1 year of age, 8 died of an infective process and 2 of renal failure. The average age at death of patients aged more than 1 year was 33 years. In 60 per cent of the cases, solitary kidney was the only congenital defect recorded.

Of the 32 cases, 20 are definitely recorded as of large single kidneys. Thompson expressed the belief that a hypertrophied kidney, although it may appear to be sound, is not a good organ so far as function is concerned. In considering the vascular supply, 1 case is noted in which there was definite segmental arrangement of the arteries.

The right kidney was more frequently absent in the males than in the females, and vice versa in the case of the left kidney. The presence of two ureteral orifices does not necessarily indicate the presence of two kidneys, and cystoscopy previous to an urgent operation may be useless or misleading unless catheterization is carried out. In any question of removal of an injured kidney in emergency, the surgeon may palpate for the presence of the other kidney.

*Ptosis*—Thomas<sup>8</sup> stated that it is doubtful whether the potential danger of movable kidney, with its insidious, symptomless destruction of the kidney by progressive hydronephrosis or infection, is always completely acknowledged by the general practitioner. Hinman, in 105 cases of hydronephrosis, reported urologic evidence of nephroptosis in 90. The majority of Thomas' series of 75 patients with nephroptosis exhibited pyuria of some degree, the complication of pyelitis was not recorded unless, by ureteral catheterization and the usual pyelographic evidence, the kidney was proved to be the source. There were 18 cases of pyelitis, 3 of pyelonephritis and 2 of pyonephrosis. Other pathologic complications were hydronephrosis, 19 cases, calculi 10 cases, and tumor, 1 case. The 75 cases may be divided into (1) simple ptosis, unilateral or bilateral, treated palliatively or operatively, (2) those

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<sup>7</sup> Thompson, A. R. Solitary Kidney, *Guv's Hosp Rep* **79** 207 (April) 1929.

<sup>8</sup> Thomas, B. A. Observations on the Diagnosis and Treatment of Movable Kidney, *J Urol* **22** 603 (Dec) 1929.

associated with hydronephrosis, (3) those associated with pyelitis, pyelonephritis or pyonephrosis, (4) those associated with calculi, and (5) those associated with tumor

Symptoms, in these cases, dated back from a few hours to forty years. Urinary symptoms and renal or lumbar pains occurred with almost equal frequency in from 80 to 85 per cent of patients, while gastro-intestinal and nervous disturbances were found in only about 20 per cent. To determine the degree or extent of mobility of a kidney accurately, pyelography is essential and must be done with the patient in both the erect and prone positions. Complete reliance should not be placed on characteristic symptoms such as discomfort, dull or severe pain in the renal areas, gastric disturbances, neurosis or the demonstration of a palpable or movable mass in the loin.

In the treatment of nephroptosis, each case should be studied separately to determine the most appropriate and best procedure. The outstanding object must be relief of the subjective symptoms as well as the prevention of the destruction of the kidney by hydronephrosis and infection. Palliative treatment is indicated in mild cases, especially those associated with general visceroptosis, when the subjective symptoms are relieved by rest or abdominal supports. Palliative treatment is contraindicated when any subjective symptoms are not completely relieved by supportive appliances, when the threat of renal injury from urinary retention and infection is uncontrolled by apparatus, when severe pyelitis, pyelonephritis, pyonephrosis, calculus or tumor coexists, when rotation of the kidney, torsion of the pedicle or fixation of a kinked ureter is present, when harmful traction is exerted on other organs, and when the kidney is movable to more than the first degree.

The mortality of nephropexy for nephroptosis is practically nil. Edebohl's claimed only 1.65 per cent in 864 cases, and Kelly 0.4 per cent in 245 cases. In Thomas' series there were no deaths. When the disease is allowed to progress to the destruction of the kidney, necessitating nephrectomy for treatment, the prognosis becomes grave. Nephropexy for ptosis in 19 cases of this series has been successful except in 1 case. Failure should never exceed 10 per cent, which represents a large measure of surgical success as compared with the results of palliative treatment. Surgical failures can be ascribed usually to faulty technique in fixation of the kidney, the incomplete removal of fatty tissue between the posterior surface of the kidney and the lumbar muscles to which it is to be fixed, failure thoroughly to mobilize the kidney and ureter and free them from any adjacent adhesions or fascial restrictions, and too short confinement to bed after operation. The

patient should be kept in a recumbent position for about a week, should not lie on the unaffected side for two weeks, may sit up in bed in three weeks and should not be allowed out of bed for four weeks. Vague pains may persist for six months after the operation.

Braasch<sup>9</sup> is of the opinion that too much enthusiasm for fixing floating kidneys may result in unwarranted nephropexy. About twenty-two years ago, during an era of nephropexy, a series of patients with floating kidneys were operated on at the Mayo Clinic. Many of these patients returned two or three years later without improvement in symptoms, or they claimed that the pain had shifted to the other side. On account of these unfavorable results, such operations were discontinued. According to Braasch, there are unquestionably movable kidneys which if fixed would relieve the patient's symptoms. Nephropexy may be indicated when pyelographic evidence demonstrates definite ureteral obstruction with resulting pyelectasis, and when there is permanent acute angulation as the result of nephroptosis, provided all other abdominal lesions have been excluded, the patient is not considered neurotic, and the other kidney is not similarly affected. Often the urogram will show dilatation not only in the renal pelvis, but of the entire ureter, without any evidence of obstruction. In such cases an atonic condition is probably the predominating factor and cannot be relieved by nephropexy. In other cases the pyelographic evidence may show minor changes which make one doubtful as to the existence of obstruction.

Mathé<sup>10</sup> described two types of movable kidney responsible for the definite clinical entity characterized by lumbar pain, loss of weight, and urinary, gastro-intestinal and nervous disturbances, which require surgical fixation. The first group consists of the infected kidney presenting pyelonephritis which, after it has acquired the lower position has become anchored in place by adhesions to the surrounding structures. In this type of ptosis a supporting belt, instead of elevating the kidney overrides and irritates it, and fails to give relief. The second type of movable kidney requiring surgical relief is the one in which the kidney, in dropping, causes the ureter to be arrested, compressed or kinked over fibrous bands or an aberrant blood vessel.

Lewis<sup>11</sup> stated that although kidneys have been unnecessarily anchored, there have also been many unnecessary operations of

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9 Braasch, W. F., in discussion on Thomas (footnote 8, p. 685)

10 Mathe, C. P., in discussion on Thomas (footnote 8, p. 691)

11 Lewis, Bransford Crowell A. J., and Quinby W. C., in discussion on Thomas (footnote 8, p. 683)

appendectomy He has observed many cases in which the appendix was removed when the real condition was nephrosis and backward pressure in the ureter

Crowell<sup>11</sup> has had excellent results following nephropexy, and he does not hesitate to perform it in properly selected cases

Quinby<sup>11</sup> stated that cases occur in which there is a rather sudden onset of acute renal pain which is undoubtedly due to an abnormally movable kidney In such cases dilatation of the renal pelvis or ureter cannot be demonstrated, but there will be delayed emptying time of the pelvis During the last four or five years he has observed from 12 to 17 such patients in whom time has proved that nephropexy effected cure

Lowsley<sup>12</sup> stated that the indications for operation on nephroptosis are direct and simple When bilateral nephroptosis is present, operation is contraindicated This condition is usually associated with enteroptosis, and operation may add to the pain instead of relieving it There is a certain amount of pull on all the viscera which extends to the attached, suspended kidneys, this increases rather than diminishes the pain In cases in which one kidney is down, and symptoms of colic and hydronephrosis are associated, if a definite diagnosis has been made, palliative treatment, including belts and irrigation of the renal pelvis, is first attempted If these measures fail to give relief and the pain referable to the kidney still persists, nephropexy is indicated Lowsley suspends the kidney in such a manner that he is reasonably sure it will not come down It is extremely important to keep the patient in bed long enough after the operation so that the tissues may become firmly healed The minimal time is three weeks and sometimes longer A long vacation after the operation is desirable

[ED NOTE—As pointed out by Braasch, indiscriminate nephropexy as done twenty years ago led the operation into deserved disrepute Nevertheless, the recent reapplication of the operation in selected cases may not be without clinical merit Mathé and Lowsley contended that suspension and fixation may gain satisfactory results if meticulous care is taken as to the type of case in which the procedure is applied As mentioned elsewhere in this review, ectopic kidneys with a concomitant ectopic blood supply and short ureters are unsuitable for renal suspension or fixation If there is general visceroptosis with bilateral nephroptosis, little can be expected from operation except an aggravation of an already distressing pathologic condition On the whole, Braasch's conservative attitude is to be recommended He would reserve surgical fixation for such cases in which there is definite ureteral obstruction with pyelectasis, or in which there is permanent acute angulation of the

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<sup>12</sup> Lowsley, O S, in discussion on Thomas (footnote 8, p 690)

ureter. He also emphasized the fact that other abdominal lesions must be definitely excluded, and that neurosis as a factor must be adequately ruled out before major surgical procedures of this type are undertaken.]

*Hydronephrosis*—Von Lichtenberg<sup>13</sup> stated that in cases of double kidneys operation can be performed either on the ureter or on the pelvis of the kidney. In case of bifid ureter part of the kidney with its respective ureter may be resected. In case of double ureter, one ureter may be implanted either into the pelvis of the kidney or into the other ureter. The ureter of the diseased half of the kidney is the one which is resected and implanted. The essential steps of the operation are described as (1) careful preparation of the hilus and the ureter, (2) amputation of the ureter at the point of origin leaving little redundant tissue in order to prevent the formation of a stricture, (3) closure at the point of the amputation, (4) resection of the redundant ureter, (5) implantation into the pelvis of the kidney or end-to-side implantation into the retained ureter above the site of crossing and (6) drainage by nephrostomy for prevention of tension on the suture line. The double pelvis may be anastomosed either with or without the resection of the extra ureter and the diseased half of the kidney may then be resected. In cases of double kidney, resection should be done if the extent of pathologic processes permits. The resection usually is bloodless and the resected half attached only to the ureter is drawn out of the operative field. Small bleeding vessels are then ligated. The two leaves of the capsule are brought together so that the line of ablation is completely covered. The free edges of the leaves are placed in the wedge formed by the resection sewed together and closely approximated by two or three through-and-through sutures.

In plastic operations for urinary obstruction the obstruction must be either radically eliminated or circumvented. In disorders such as accessory arteries and kinks a plastic operation is not necessary. In the remaining cases the relief of the obstruction is associated either with the transverse or the lateral incision of the ureter. Topographically three types of obstruction are differentiated depending on the site of the lesion: those at the ureteropelvic juncture, those along the course of the ureter and those in the intramural portion of the ureter and at the opening into the bladder. If a stricture is found to be close to the ureteropelvic juncture the stricture should be resected and the ureter implanted into the pelvis.

Von Lichtenberg implants the ureter in the following manner. A no. 12 to no. 14 rubber catheter is inserted in the ureter for from 5 to 6.5 cm. and fixed by a few sutures. The point of ablation of the strictured

<sup>13</sup> Von Lichtenberg, Alexander. Plastic Surgery of the Renal Pelvis and Ureter. J. A. M. A. 93:1705 (Nov. 30) 1929.



area of the ureter at the ureteropelvic juncture is then widened and, with long, thin, curved forceps, the catheter is drawn through the lowest calyx and the lowest portion of the parenchyma of the kidney. The catheter is fixed with a suture in such a position that it enters the pelvis of the kidney for 2.5 cm. Two lateral openings are previously made in that portion of the catheter which is to lie in the pelvis of the kidney, to insure perfect drainage. The pelvis is then sewed to the ureter in the form of a cuff, and the remaining open pelvis is closed with a few sutures. If the exit of the ureter from the pelvis is congenitally abnormal, the part is excised by a circular incision, the pelvis is closed, and the ureter is reimplanted in correct position lower down. If the radical removal of the obstructing cause is not practicable, ureteropyeloneostomy may be done as a palliative operation. For this von Lichtenberg uses an original method which is allied to the Finney gastroduodenostomy and which has given excellent operative and postoperative results.

Von Lichtenberg presented the results of 80 operations for renal obstruction in patients who were treated over a period of two years. In 41 per cent, the kidney had to be removed because the obstruction was complete. In 47 cases (59 per cent), treatment was conservative. In 23 cases, mechanical obstruction could not be found. In 27 per cent of these cases, the obstruction was of neurogenic origin. In 12 cases, nephrectomy was performed. Fenger's operation was performed in 10 cases. In 1 case, the operation was combined with pyeloplasty. Congenital abnormalities were found in 20 cases (25 per cent). Abnormal insertion occurred in 3 cases, hypoplastic kidney in 2 cases and accessory vessels in 15 cases. Nephrectomy was performed in 10 of these cases (50 per cent), a neoimplantation of the ureter was done in 1 case, and dissection of an accessory vessel was done in 9 cases. There were strictures of the ureteropelvic juncture in 37 cases. In 11 cases of ureteropelvic obstruction (30 per cent) nephrectomy was performed, in 9, ureteropyeloneostomy, in 11, Fenger's plastic operation, in 2, neoimplantation, and in 4, surgical dilation of the ureter. Among the 47 cases in which conservative operation was done, secondary nephrectomy was performed in 3 (7 per cent). Death did not occur in any of these cases.

[ED. NOTE.—Plastic operations on the ureter and renal pelvis have been gaining in favor both in this country and in Europe during the last few years. Ten years ago such operative procedures sometimes made subsequent nephrectomy necessary, and they were held in bad repute. Recently, the work of Quinby, Young and Walters has offered much promise. Von Lichtenberg's method of ureteral implantation by splinting the site of anastomosis with a catheter which provides urinary drainage through the pelvis of the kidney during the time of healing

seems to be based on sound surgical principles. Furthermore it is in accord with the experiments on shunting the flow of urine from the site of ureteral anastomosis which have been described a number of times in American literature during the last two years.]

Quinby<sup>14</sup> stressed the importance of constructive and safe operation when possible. Lack of familiarity with the possibilities of conservation offered by plastic operations on the kidney, ureter and pelvis, or a lack of knowledge of the technic of such operations is mainly responsible for too many nephrectomies having been performed in the past. In general the renal conditions which are most frequently amenable to plastic surgery are those in which stasis of urine within the pelvis of the kidney or in the ureter has taken place. A more comprehensive understanding of the dynamics of the ureter with regard to their application to clinical and pathologic phenomena is aiding in the explanation of many instances of apparent stricture or vesical reflux and ureteral retroperistalsis. Normal peristalsis of the ureter is now known to begin in the pelvis of the kidney and is propagated downward to the bladder. It has been demonstrated that hydronephrosis can be caused experimentally by inhibition of peristalsis without any mechanical obstruction of the lumen of the ureter. In other words the ureter is composed of smooth muscle fibers, and their reaction to many forms of stimuli is known to be extremely labile.

In view of these known facts Quinby suggested that the cause of the hydronephrosis associated with an abnormality of the blood supply is to be found in the pulsations of the artery itself lying in juxtaposition to the ureter and inhibiting there the normal flow of peristaltic waves. Mechanical obstruction is not necessary; the current of action set up by each arterial beat is sufficient to cause nervous interference of a minor degree in the ureter.

The pelvis of the kidney dilates slowly and progressively from birth and finally symptoms appear. Many of these patients date the onset of symptoms at some period during their second ten years of life.

Six patients operated on during the last two years for hydronephrosis convalesced normally. Investigation of 16 cases of plastic operations on the kidney had shown that in every instance the function of the kidney operated on has improved.

[ED. NOTE—For years Quinby has been most insistent on conservative plastic operations in cases of hydronephrosis and obstructive disease in the kidney and ureter. As a pioneer in this field his work has been stimulating to those who are following, modifying and sup-

<sup>14</sup> Quinby, W. C. Factors Influencing the Operative Procedure in Hydronephrosis, J. A. M. A. 93:1709 (Nov. 30) 1929.

plementing his technic Doubtless great development and simplification of technical procedure will come within the next few years, with the result that fewer radical total nephrectomies will be performed ]

Walters and Braasch<sup>15</sup> reported on 10 plastic operations for hydronephrosis performed on 9 patients at the Mayo Clinic In 1 of the 4 cases in which a hydronephrotic renal pelvis was resected, the operation was bilateral Four of these 5 resections were successful, secondary nephrectomy was necessary in the other case In the case in which resection was bilateral, with an interval of four months between operations, results in both kidneys were excellent Resection of the hydronephrotic or pyonephrotic portion of a duplicated kidney was performed in 3 cases Ureteropyeloneostomy for obstruction at the ureteropelvic juncture was done in 2 cases, in 1 of these, the obstruction involved a solitary kidney and was acute and complete, in the other, the obstruction followed pelviolithotomy performed elsewhere

The value of plastic procedures on the kidney, pelvis and ureter from which the outflow is obstructed is illustrated in 2 of the cases reported by Walters and Braasch in which the plastic operations were necessary In 1 instance, the hydronephrosis was bilateral with extensive dilatation and considerable infection, in the other, the obstruction of the ureteropelvic juncture was complete and the kidney was solitary In only 1 of the 9 cases was secondary nephrectomy necessary, in this case the hydronephrotic pelvis was of a capacity of approximately 450 cc, and infection and edema caused obstruction of the ureteropelvic juncture The decision for resection of the renal pelvis rather than nephrectomy was probably inadvisable because of the extreme degree of hydronephrosis and of obstruction of the renal parenchyma The other patients recovered, urinary drainage and renal function were satisfactory Postoperative urographic examination showed that the renal pelves were approximately normal

[ED NOTE—This work is in line with that of von Lichtenberg and Quinby and shows a definite trend toward conservative plastic operation in dealing with urinary obstruction The recent reports of plastic operations on the renal pelvis and ureter show results which are not ideal, but are much better than those obtained a few years ago when such procedure was usually an unintentional preliminary step to nephrectomy With improvements in technic such plastic operations should gain favor

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15 Walters, Waltman, and Braasch, W F Urinary Obstruction and Hydronephrosis, J A M A 93 1710 (Nov 30) 1929

with urologists in general and thus offer a definite opportunity for saving functioning renal tissue which would otherwise be sacrificed ]

Herbst and Polkey<sup>16</sup> undertook an investigation on dogs to determine the probable value of Fenger's operation for relief of hydronephrosis due to stricture. Failure of the operation was noted in a large percentage of clinical cases, some of the cures reported in the literature were probably only symptomatic, not actual. The operation was uniformly unsuccessful in a series of 16 dogs, due to mechanical buckling at the site of operation and increased scarring which produced obstruction. Herbst and Polkey concluded, therefore, that ureteropyeloplasty is not a reliable method to be used for the relief from hydronephrosis due to stricture at the ureteropelvic juncture, a conclusion that had been borne out by the clinical experience of many who have utilized this method.

Herbst and Polkey expressed the belief that some form of anastomosis between the pelvis and ureter will give better results than plastic procedures in this type of obstruction. Clinical facts pertaining to such anastomoses are limited and a study is being conducted on the dog to determine, if possible, which of the various methods offers the best chance of success.

Patch<sup>17</sup> stated that the increasing tendency toward conservatism in renal surgery is a principle particularly applicable in cases of hydronephrosis associated with aberrant renal vessels, especially of the lower pole. When hydronephrosis exists to a degree of complete or almost complete renal atrophy, nephrectomy is indicated. In cases in which considerable renal tissue remains, treatment should be directed toward relief of the obstructive condition producing stasis, as well as toward conservation of the kidney. Unless obstruction is relieved, further extension of the hydronephrosis and destruction of the kidney will result. Experimental and clinical evidence shows that ligation of a renal vessel is followed by necrosis of the renal tissue supplied by the vessel. In one of Patch's cases in which a small vessel of the lower pole was ligated, the patient died a few months later from intercurrent disease. Examination of the kidney revealed necrosis of the segment of kidney supplied by the ligated vessel. The renal necrosis following ligation is usually aseptic, but secondary suppuration of the infarcted portion of

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16 Herbst, R. H., and Polkey, H. J. Fenger's Uretero-pyelo-plastic Operation. An Experimental Study, *J Urol* 23:23 (Jan) 1930.

17 Patch, F. S. Conservative Plastic Surgery in the Treatment of Hydronephrosis Associated with Aberrant Vessels. *Brit J Urol* 1:373 (Dec) 1929.

the kidney may follow. The practice of ligating an aberrant vessel is not recommended because of the risk of the procedure.

Patch noted 3 cases within the past eighteen months in which aberrant vessels entering the lower pole seemed to be the prime factor in producing hydronephrosis. Section and reimplantation of the ureter in a position out of contact with the vessel and in a position favorable to drainage was done by Giegoue in 1 case and by Quinby in 7 cases without technical difficulty and with apparent success. In Patch's series relief of the obstruction, as well as conservation of the kidney and the arterial supply of considerable segments of the kidneys, was definitely indicated. Nephropexy did not seem desirable. In all 3 cases section was made of the pelvis, and the cut ends were resutured out of contact with the vessel. Making the incision in the pelvis in which the lumen is larger is more advantageous than in the narrow ureter, with the danger of block by edema, or subsequently by stricture. Only ordinary and transient drainage of the wound was instituted. In no instance was there any complication by leakage or infection, and the patients were all relieved of symptoms.

The technical difficulties in performing the operation and in securing primary union were not great. In one case in which ptosis of the kidney was associated with an aberrant artery, nephropexy was not combined with ureteral implantation because of hesitancy to complicate the operation and because it was desirable to test the efficacy of reimplantation. In choosing between nephropexy and ureteral reimplantation, the latter seemed to be the procedure promising the greatest degree of relief to the urinary stasis. In view of the ease and safety of the operation and the experience gained, Patch would not hesitate to combine the two procedures or to carry out other plastic measures designed to decrease the size of the dilated pelvis and to improve urinary drainage.

Ferrer<sup>18</sup> stated that total renal compression is the result of chronic renal obstruction. Partial renal compression, such as that produced by tumors of one pole of the kidney or stones in the kidney, or the minor or major calices, will not by itself produce true hydronephrosis. Bilateral hydronephrosis occurs only when obstruction is in the lower part of the urinary tract. This obstruction reflects back pressure on the pelvis and, if free collateral venous circulation is formed on or around the capsule of the kidney, pressure atrophy will take place in the renal substance, with the formation of atrophic hydronephrosis. When this type of hydronephrosis is established, the atrophy will take the form and shape of the venous arches that surround the superior portion of each renal papilla.

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18 Ferrer, J. C. Renal Compression, *J. Urol.* **22** 453 (Nov.) 1929

*Stone*—Keyes<sup>19</sup> reported on the results of operations on 6 patients who had only 1 kidney, 5 operations were performed for stone and 1 was performed for acute suppuration. Decapsulation was performed in a case of acute suppurative nephritis, pyelotomy was performed in 1 case, and pyelonephrotomy in 4. None of the stones was large. The patients have survived from a few months to thirteen years. Roentgenograms after operation did not reveal stone. One patient who began to pass stones from five to ten years after the last operation has had 3 operations on a single kidney. Another patient has had 2 operations. The convalescence of these patients did not differ materially from that of similar patients with 2 kidneys. One patient with acute suppurative nephritis was so sick that when she recovered from decapsulation she had no recollection of the day before the operation. After decapsulation, her temperature became normal and her mind clear. In the cases of stone, operation was done for anuria in 4 cases and for persistent pain in 1 case. At the time of operation the anuria had lasted one, two, four and six days, respectively.

Two special precautions are taken in operating in cases of this type in the hope of minimizing postoperative renal congestion: the pyelotomy incision is left unsutured, and the kidney is decapsulated. There has been no alarming failure of renal function after operation. Keyes attributed the fact that these patients stand operation almost as well as patients with two kidneys to the gentle handling of the kidneys and to a less severe immediate postoperative reaction in already infected kidneys than occurs in operations on normal renal parenchyma.

Walters<sup>20</sup> reported on 43 operations in cases of solitary kidney or ureter at the Mayo Clinic. Thirty-five of these operations were for stone, in 8 cases ureterolithotomy was performed. The operative mortality in the entire group was 14 per cent, whereas the 8 operations on the ureter were done without mortality. The patients who failed to recover had varying degrees of renal insufficiency and infection, and died in uremia. He emphasized the necessity of early operation for the removal of stones in a solitary kidney and ureter before renal infection and decreasing function increase the risk of the operation. The patient should be reexamined at frequent intervals, especially if urinary lithiasis has been a complication.

*Tumor*—Judd and Hand<sup>21</sup> reviewed 367 cases of carcinoma of the kidney observed at the Mayo Clinic over a period of twenty-seven

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19 Keyes, E. L. Operation on the Single Kidney, Especially for Stone, *J. A. M. A.* **94** 152 (Jan. 18) 1930.

20 Walters, Waltman in discussion on Keyes (footnote 19, p. 155).

21 Judd, E. S. and Hand, I. R. Hypernephroma, *J. Urol.* **22** 10 (July) 1929.

years Two hundred eighty-three of the 312 patients who underwent nephrectomy and 47 of the 55 who were submitted to exploration have been traced

These carcinomas of the kidney appear as soft, roughly spherical grayish-yellow growths, often hemorrhagic, and associated with tortuous, dilated superficial veins In the series of 283 cases the carcinomas were confined to the upper pole in 51 cases, to the lower pole in 60, and to the median renal region of the kidney in 39, the entire kidney was involved in 10, and the involvement was not recorded in 123 The capsule was ruptured in 104 of the cases, and the renal veins were involved in 51 Metastasis was observed in 98 cases Occasionally, significant symptoms did not appear until the tumor was unusually large The lesion involved the right kidney in 169 cases and the left kidney in 196 In 2 cases the side involved was not stated One hundred and sixty-one patients noted the first symptom before the age of 50, 203 noted it after 50, the age of 3 was not recorded The average duration of symptoms and the average postoperative length of life, both of the patients who died and of those living, is less for females than for males, suggesting that malignancy runs a more rapid course in females

Hematuria was the first symptom in 43.86 per cent of the entire series of 367 cases Pain was the initial symptom in 37.32 per cent of the cases, a tumor was the first symptom in 13.62 per cent, and weakness was given as the first symptom in 3.26 per cent Hematuria occurred in 69 per cent, and a tumor was noted in 80 per cent Chills, fever and night sweats were present in about 10 per cent of the cases, indicating that the patient may have been reacting to a certain degree of pyelonephritis Pain occurred in more than 80 per cent of the cases When the tumor was large enough to be palpated, and when it had become fixed, the mortality rate increased The size of the tumor bears a definite relationship to the postoperative length of life The immediate risk of the operation is greater if the tumor is large If the tumors were small the patients lived considerably longer than if they were of moderate size or large

There was extension to the renal vein in 51 of the cases in which nephrectomy was carried out, 9 of these patients are still living Judd and Hand concluded that in cases in which the tumor can be removed without too great risk, it should be done in spite of the involvement of the vein and pedicle

If the tumor is large, the usual posterolateral incision may be enlarged enough to give satisfactory exposure The skin, fascia and lateral abdominal muscles are cut, and posteriorly the quadratus lumborum and the costovertebral ligament may be divided this mobilizes

the lower part of the thorax. In many of these cases it may be advantageous to fracture the lower rib by simply retracting it with the hand. The peritoneum is retracted away from the tumor, which usually bulges well forward. Retraction of the peritoneum permits exposure of the vascular pedicle and examination of the regional lymph nodes. As soon as the tumor has been mobilized and lifted away from the perirenal tissue, the exposure is completed. The kidney is generally adherent to the fatty capsule and is covered with large dilated veins. Usually it is advisable to ligate the pedicle and to remove the clamps, if a large mass of tissue is clamped and the tissues are edematous and friable, this is not always safe. In about 10 per cent of the cases it seemed best to leave the clamps on the vascular pedicle for seventy-two to ninety-six hours. Following nephrectomy alone, 3 patients returned because of recurrence in the ureter. Removal of the upper part of the ureter is indicated in all cases of malignant renal neoplasms but its entire removal is not indicated in cases of this type.

Metastasis is common, progresses slowly, and is difficult to recognize. It may not cause trouble until years after the primary focus has been recognized and treated. Metastasis to the lung is most common. Minute foci occur which are not distinguishable in an ordinary roentgen examination of the lungs. Definite metastasis occurred in 70 patients of this series, it was in the lungs in 39, in the liver in 13, in the brain in 5, and in the bones in 11.

Eighteen men and 8 women had lived ten years or more. The average age of the men was 49 years and of the women 48 years at the time of operation. The right kidney was involved in 15 cases and the left in 11. The average duration of symptoms was slightly more than three years before operation. The first symptom in order of frequency was pain in 12 cases, hematuria in 9, and tumor in 2. A palpable tumor was demonstrated at the time of operation in 11 cases. The tumor was reported as large in 13 cases. The longest length of life after operation for alveolar carcinoma in the series was six years and ten months, and after operation for hypernephroma, twenty-two years and eight months.

Judd and Hand concluded that carcinoma of the renal cortex is extremely malignant and often is well advanced before symptoms are noticeable. Alveolar carcinoma is the most highly malignant of the various types of renal carcinoma whereas adenocarcinoma is less malignant, judging from the clinical course. Because 106 of the patients of their series lived from three to twenty-two years Judd and Hand are of the opinion that operation will result in cure in a definite proportion of cases.

[ED. NOTE.—This study bears out contemporary concepts of renal neoplasia so far as relative malignancy of sarcoma, carcinoma, and



hypernephroid types of renal tumors is concerned. The fact that surgical treatment of 367 cases resulted in prolonging the life of 106 patients affords a hopeful outlook. The use of radiotherapy, either preoperatively or postoperatively, is not mentioned. The fact seems well established that as yet in this field of neoplasia little may be expected of such physical agents.]

Kukudschanow,<sup>22</sup> in studying renal parenchyma in association with tumorous conditions, noted that the changes may vary within wide limits, but usually it remains unchanged. The pathologic-anatomic changes in the kidney are about 60 per cent nephrotic and 50 per cent interstitial. Only rarely is the entire kidney affected, the condition usually being local. The changes are commonly noted in the cortex. Sclerosis of the vessels is frequently noted (70 to 75 per cent). Focal conditions of a nephrotic nature may occur (20 per cent). Functional disturbances of the kidney are absent, or, if present, are only moderate. There is no connection between the size of the tumor and the severity of parenchymal changes. In cases in which only a sixth to an eighth of the parenchyma of the kidney remains, there is severe parenchymal change. The parenchyma not affected by the tumor may be disturbed by pressure of the tumor, stasis of blood, retention of urine or by the toxic products of the tumor. These factors may occur one or more at the same time, whereas in the later stages they may be superimposed on one another.

Schmidt<sup>23</sup> reported on a series of 71 cases of tumor of the kidney. Twenty-three of these cases were not considered because operation had been performed elsewhere or a histologic examination was not made. Of the remaining 48 cases of tumor, 3 were benign and 45 malignant. The tumors comprised 6.14 per cent of all diseases of the kidney in which treatment has been given. The benign tumors were papilloma of the renal pelvis, papillary adenoma of the kidney and papillary cystadenoma of the mucous membrane. The malignant tumors consisted of 29 hypernephromas, 6 carcinomas, 1 papillary carcinoma of the pelvis of the kidney, 3 renal sarcomas, 1 suprarenal sarcoma and 5 congenital mixed tumors in children. From an analysis of this material it was concluded that neither the duration nor the frequency of the classic symptoms, such as palpable tumor, hematuria and pain, was any criterion of the growth or spread of the tumors. Neither were the operative data an indication as to prognosis. The size or

22 Kukudschanow, N. J. Die Veränderungen der Niere in der weiteren Umgebung der Affektionsstelle bei Nierengeschwulsten, *Ztschr. f. urol. Chir.* **27** 337 (July) 1929.

23 Schmidt, A. Der Wert der klassischen Nierentumorsymptome für die Frühdiagnose, *Beitr. z. klin. Chir.* **145** 48 (June) 1928.

malignancy of the individual tumors might indicate some idea as to expectancy of life. Schmidt does not believe that cardinal symptoms are necessary for diagnosis and when present usually indicate an extensive growth. A cystoscopic examination was made in 70 per cent of the cases. In 29 per cent of the cases the bleeding side was noted directly. In 73 per cent of the cases renal function, as determined by return of indigocarmine, aided in indicating the affected side. In 10 cases pyelography gave diagnostic aid. Pneumoradiography, according to Rosenstein, gave excellent service in doubtful cases, such as in distinguishing between a renal tumor and spleen.

*Tuberculosis*—Medlar<sup>24</sup> expressed disagreement with the two prevalent ideas that excretory bacilluria exists without tuberculous lesions in the kidney and that tuberculosis of the kidney never heals. All obtainable evidence points to the fact that renal tuberculosis is a hematogenous infection and that it is but one manifestation of general tuberculosis. In some cases the major tuberculous lesion occurs in the kidney. From a study of the urine of animals experimentally infected with bacilli of tuberculosis, evidence was not found to support the view that the kidney excreted the bacilli without tuberculous lesions of the ulcerative type being present in the organ. When bacilli of tuberculosis were demonstrated in the urine, ulcerative tuberculous lesions in the kidney were present. The conclusions were that the bacilli were not excreted by noninfected kidneys and that their absence in the urine did not necessarily eliminate the presence of tuberculous lesions in the kidneys.

In the investigation of the healing of tuberculous lesions in the kidney, 30 cases in which death occurred from pulmonary tuberculosis were studied, emphasis being placed on cases in which lesions were small rather than on those that were large and were noted late in the course of the disease. It was found that the kidneys are commonly involved in fatal cases of pulmonary tuberculosis. The renal lesions are hematogenous in origin, and both kidneys are usually involved, although one may be more extensively involved than the other. Scars were demonstrated in a considerable proportion of those kidneys in which definite tuberculous lesions were also present. These probably represent healed tuberculous lesions although there is nothing pathognomonic of their having been tuberculous. Medlar expressed the belief that a kidney with a large tuberculous lesion will completely heal and that it is possible for it to become less active and regress in its progressive character.

[ED. NOTE—For many years the contention that healing never occurs in renal tuberculosis has been accepted as axiomatic. Sporadic

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<sup>24</sup> Medlar, E. M. The Pathogenesis of Renal Tuberculosis, *Am. J. Surg.* 7: 605 (Nov.) 1929.

reports of healed tubercle in the kidney have been received with skepticism. Recently the work of Thomas and others has thrown some doubt on the matter. Hence Medlar's observations in cases of pulmonary tuberculosis coming to necropsy are in line with the later conception of the possibility of healed renal tuberculous disease. From the practical point of view, it is still likely that the practice of most urologists will be nephrectomy in unilateral renal tuberculosis if the process is at all advanced. Certainly such patients if treated surgically or otherwise should have at once the advantages of treatment in a sanatorium. If the disease is bilateral, the indications for operation are more limited. In very early unilateral disease conservative medical treatment should be employed only if the patient is under frequent observation by a urologist and is being treated under sanatorium conditions.]

Olsen<sup>25</sup> stated that renal tuberculosis and associated renal lesions is not uncommon, some of the coexisting lesions cited were true renal stones, leukoplakia of the renal pelvis, solitary cyst of the kidney and adenocarcinoma. To avoid classification of all the symptoms under one disease, a careful, complete preoperative urologic investigation, together with thorough pathologic studies, is urged.

Thomas,<sup>26</sup> in a recent review, observed that from 25 to 35 per cent of all nephrectomies are done because of renal infection caused by the bacillus of tuberculosis. Forty per cent of such patients are not cured by nephrectomy but continue to have persistent symptoms referable to the bladder, the condition for which many are seeking relief.

Certain pathologic types are recognizable: (1) in toxic albuminuria without casts, few if any pus cells in the urine, and if ulceration occurs it may contain bacilli of tuberculosis, (2) in subacute and chronic nephritis albumin and casts in the urine, bacilli of tuberculosis may be present and pus cells frequently are present, (3) hemorrhagic nephritis characterized by blood cells in the urine, light albuminuria and a few casts, and (4) amyloid degeneration, a type glomerulonephrosis which is possibly the result of inflammatory reaction in the kidney caused by the bacillus of tuberculosis directly, or by toxemia caused by tuberculous infection elsewhere.

In the majority of cases, renal tuberculosis is a bilateral condition. Repeated examinations are necessary to prove the presence of a non-destructive tuberculous infection in an apparently sound kidney. One infected kidney should not be removed until it has been proved conclusively that the other does not contain a destructive lesion. Non-

25 Olsen, Sidney. Associated Renal Pathology in Renal Tuberculosis. *J Urol* 23: 81 (Jan) 1930.

26 Thomas, G. J. Renal Tuberculosis. *J A M A* 94: 229 (Jan 25) 1930.

destructive lesions will heal, and the patient with this type of lesion should have the advantage of treatment in a sanatorium to assist him in building up resistance against tuberculosis. Nephrectomy is not the sole treatment for renal tuberculosis. After operation, the patient should be kept in a sanatorium until no evidence of active tuberculosis can be found, urinary or otherwise.

Braasch<sup>27</sup> stated that the diagnosis of early renal tuberculosis is frequently made only after repeated inoculation of guinea-pigs or long study of the case, and the condition may easily be overlooked if only the usual clinical methods are employed. Pyelography will often demonstrate deformity in such cases, which is not apparent by other methods. Inoculation of guinea-pigs, as well as renal functional tests, are uncertain in their results. When the diagnosis is in doubt urography offers the most valuable aid. One of the greatest difficulties in the study of renal tuberculosis is to determine whether the disease is unilateral or bilateral. It has been shown recently that the results of inoculation of guinea-pigs with material from a healthy kidney is frequently positive, as the result of regurgitation of bacilli of tuberculosis from the bladder.

Frisch<sup>28</sup> stated that the diagnosis of urinary tuberculosis does not offer special difficulties unless organisms are found other than bacilli of tuberculosis. Formerly sterile pyuria was assumed to be pathognomonic of tuberculosis. It is only recently that the rôle of mixed infections has been considered. Wildbolz noted mixed infections in 22 per cent of his cases of renal tuberculosis, Runeberg noted it in 37 per cent of 2,655 cases, Suter noted 8 cases in 78, Pousson 12 in 32, and Rafin, 71 in 239.

Colombino demonstrated that in tuberculosis of the urogenital tract the leukocytes exhibit characteristic changes. In an untreated preparation of the urine, there may be seen elongated, dented or jagged forms, occasionally there may be oval protoplasmic bodies, which come from the leukocytes. After staining, many vacuoles are found about the nucleus, and the protoplasm shows marked shrinkage. If leukocytes thus formed are found in conjunction with erythrocytes, it is fairly certain that tuberculosis is present. Frisch stated that this phenomenon was present in all of his ten cases. Bacteriologic examination of the sterile urines revealed the colon bacillus in 5 cases, streptococcus in 2 cases, and staphylococcus in 3 cases. In 1 case the bacillus could not be demonstrated preoperatively. The source of these secondary infections is not known.

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<sup>27</sup> Braasch, W. F., in discussion on Thomas (footnote 26, p. 238).

<sup>28</sup> Frisch, Bruno. Ueber Mischinfektion bei Nierentuberkulose. *Ztschr. f. urol. Chir.* **27**: 248 (Mar.) 1920.

*Perinephritic Abscess*—Feci<sup>29</sup> noted that perinephritic abscess or perinephritic phlegmon may occur in the acute, subacute or chronic form. The chronic form is the more common and the most difficult to diagnose. He is of the opinion that roentgen examination may yield significant data in regard to the diagnosis. The abscess cavities were injected with a substance opaque to the roentgen rays. These data, linked with the clinical symptoms, permitted him to make a correct diagnosis in 2 cases.

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<sup>29</sup> Feci, Lorenzo. Contributo radiologico alla diagnosi degli ascessi perirenali, Arch ital di urol 4 503 (Aug) 1928

*(To be Continued)*

## CONGENITAL INSUFFICIENCY OF THE PALATE \*

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*He who knows the past can best interpret the present*

English	Congenital insufficiency of the palate Congenital shortening of the palate Submucous cleft palate
French	Brievete velo-palatine Insuffisance velo-palatine
German	Submukoese Spaltung des harten Gaumens Fissura ossea occulta Fissura muscularis occulta
Italian	Insufficienza velo-palatina

Congenital insufficiency of the palate is a condition in which the velum, assisted by the superior constrictor muscle of the pharynx, fails to produce sphincter-like closure between the nasopharynx and the oropharynx, a condition essential for the production of normal speech. While congenital insufficiency of the palate has probably existed from the beginning of the human race, no reference to it occurs in the literature until 1825.

Roux,<sup>1</sup> in 1825, first called the attention of the medical profession to congenital insufficiency of the palate. He stated in his paper that in 1823 he was consulted by a young girl who nasalized so badly that her speech was unintelligible. He described in this girl a cleft of the posterior portion of the velum, and stated that there was faulty union of the osseous tissue of the hard palate under an intact mucosa. As far as I have been able to ascertain by an exhaustive study of the literature, Roux was the first to describe this variety of submucous cleft palate.

\* Submitted for publication, Jan 8 1930

The artist's drawings which appear in this essay were made by Mr Erwin F. Faber of Philadelphia.

This essay was submitted for the Alvarenga Prize of the College of Physicians of Philadelphia, Pennsylvania May 1 1929. The Alvarenga Prize was awarded for this essay July 14, 1929.

1 Roux, Joseph Philibert. *Memoires sur staphylorrhachie*, Paris: J-S Chaudé, 1825, p 84.

Demarquay,<sup>2</sup> in 1846, exhibited a dissection in which there was a cleft of the velum and the bony palate, the cleft in the latter being filled with fibrous tissue, the mucosa was intact

In 1862, Passavant<sup>3</sup> described the absence of a median triangular portion of the posterior part of the bony palate. The mucosa over this portion was intact. The patient also had a cleft of the velum and the alveolar border. Passavant stated that healing occurred in the velum at the age of 15 months.

Langenbeck,<sup>4</sup> in 1864, differentiated three forms of congenital anomalies of the palate in which there was absence of bony tissue underneath the unaffected mucosa. He described the following varieties:

1 Cases of cleft of the velum in which the bony palate is almost entirely absent, although the mucosal covering is present.

2 Cases of cleft of the velum and hard palate in which the fissure in the bony palate is more extensive than in the soft parts covering the palatine vault.

3 Cases of cleft of the velum associated with a fine split either in the midline or to either side of the vomer, with the mucosa intact.

Notta,<sup>5</sup> in 1869, reported a case of a girl, aged 11 years, in whom the uvula was cleft. Under the intact mucosa there was a triangular breach in the substance of the hard palate, extending from the incisive fossa and ending posteriorly with its base in line with the last molar tooth. The patient spoke with a distinct nasal twang.

In 1869, the term "*brevete de la voûte palatine*" was introduced by Trelat.<sup>6</sup> Trelat attributed the nasal intonation to the anteroposterior shortening and lateral narrowing of the hard palate. He also recognized the association of anteroposterior brevity of the bony palate and described the notching of the palate bones toward the velum.

Gayraud,<sup>7</sup> in 1884, called the attention of the medical profession to the fact that this type of congenital anomaly, namely, anteroposterior shortening of the palate, was much more common than was hitherto supposed, and he felt that it was the chief factor in causing nasal speech. Lermoyez,<sup>8</sup> in 1892, introduced the term "*insuffisance vélo-palatine*," and in a lucid and detailed treatise described twelve cases.

The first one to call attention to the condition in America was Mears<sup>9</sup> of Philadelphia, who in 1893 reported a case in a young lady

2 Demarquay. *Bull Soc anat de Paris* **21** 11, 1846.

3 Passavant. Gustav. *Arch d Heil* **3** 334, 1862, *Arch f klin Chir* **6** 333 and 587, 1865.

4 Langenbeck. *Arch f klin Chir* **5** 7, 1864.

5 Notta. *Bull Soc de chir de Paris* (1869) **10** 419, 1870.

6 Trelat, U. *Bull Soc de chir de Paris* (1869) **10** 402, 1870.

7 Gayraud. B. *Dictionnaire encyclopedique des sciences medicale*, Paris, Masson et fils, 1884, vol 19, pp 698 and 702.

8 Lermoyez, Marcel. *Ann d mal de l'oreille, du larynx* **13** 161 1892.

9 Mears, J. Ewing. *Southern M Rec* **24** 59 1894, *Clefts of the Hard and Soft Palate*, Philadelphia, 1893.

with marked shortening of the velum and a pronounced nasal and guttural speech.

Botex<sup>10</sup> of Barcelona devised an operation in 1907 for the correction of this deformity. Further details of this operation will be discussed later in the body of this paper.

The term "submucous cleft palate" was introduced into the literature in 1910 by Kelly<sup>11</sup> of London, who made a thorough investigation of this congenital malformation and published the first complete and systematic English treatise dealing with this subject.

Scemm<sup>12</sup> of Prague contributed valuable papers on the symptomatology and pathology of submucous clefts of the hard palate.

In 1927 Limberg<sup>13</sup> of Leningrad introduced the terms "fissura ossea occulta" by which he meant submucous cleft of the hard palate, and "fissura muscularis occulta" by which he meant submucous cleft of the soft palate.

That the subject of insufficiency of the palate has attracted the attention of numerous observers is evidenced by the fact that mention of this condition has been made by every important worker in the field of cleft palate among whom are mentioned

Simon<sup>14</sup>, Ehrmann<sup>15</sup>, Wolff<sup>16</sup>, Frankel,<sup>17</sup> Kayser<sup>18</sup>, Castex,<sup>19</sup> Froschels,<sup>20</sup> Egger,<sup>21</sup> Neugenbauer,<sup>22</sup> Bonne,<sup>23</sup> Gard,<sup>24</sup> Fem,<sup>24</sup> Gutz-

10 Botex, Ricardo. Rev. de clin. med. **33** 433, 1907. Arch. Internat. de Laryng. **21** 392, 1908.

11 Kelly, A. Brown. J. Laryng. & Otol. **25** 281 and 342, 1910.

12 Scemm, Milo. Berl. klin. Wchnschr. **56** 377, 1919. Monatschr. f. Ohrenh. u. Laryngol.-Rhinol. **53** 510, 1919. Arch. Internat. de laryngol., oto-rhinol. et broncho-oesoph. **3** 388, 1924. Čes. léc. česk. **62** 461, 1923. Zentralorgan f. d. ges. Chir. **23** 457, 1923, Čes. léc. česk. **61** 811, 1922, Zentralorgan f. d. ges. Chir. **21** 179, 1923.

13 Limberg, Alexander. Zentralbl. f. Chir. **54** 1745, 1927, J. Am. Dent. A. **14** 1113, 1927.

14 Simon, Gustav. Greitswalder medizinische Beiträge, Danzig, 1864, vol. 2, p. 169, Vrtljsschr. f. d. prakt. Heilk. **1** 1, 1867, Mitteilungen aus der chirurgischen Klinik des Rostocker Krankenhauses 1861-1865, Prag, Reichenecker, 1868, p. 80.

15 Ehrmann, J. Gaz. med. de Strasb., 1880, p. 118.

16 Wolff, Julius. Verhandl. d. deutsch. Gesellsch. f. Chir. **14** 387, 1885, **23** 461, 1894.

17 Frankel. Berl. klin. Wchnschr. **19** 582, 1882.

18 Kayser, B. Deutsche med. Wchnschr., 1891, p. 825.

19 Castex, A. Ann. d. mal. de l'oreille, du larynx. **19** 415, 1893.

20 Froschels, Emil. Wien. med. Wchnschr. **61** 2537, 1911.

21 Egger, L. Ann. d. mal. de l'oreille, du larynx. **22** 365, 1896.

22 Neugenbauer, Bruno. Ueber Messungen des weichen Gaumens mit Darstellung einer neuen Messungsmethode, Inaug. Diss., Koenigsberg, 1896.

23 Bonne, Andre. De la Rhinolalie, These de Lyon, 1897, no. 92.

24 Fem, Johann. Wien. klin. Wchnschr. **12** 76, 1899, **9** 982, 1896.



mann,<sup>25</sup> Geisuny,<sup>26</sup> Lannois,<sup>27</sup> Chiari,<sup>28</sup> Helleu,<sup>29</sup> Philip,<sup>30</sup> Rouvillois,<sup>31</sup> Brown,<sup>32</sup> Stimson,<sup>33</sup> Foucou,<sup>34</sup> Blair,<sup>35</sup> Roberts,<sup>36</sup> Moure,<sup>37</sup> Grunberg,<sup>38</sup> Peter,<sup>39</sup> Kenyon,<sup>40</sup> Stern,<sup>41</sup> Imhofer,<sup>42</sup> Franke,<sup>43</sup> Bumba,<sup>44</sup> Apert and Bigot,<sup>45</sup> Rabattu,<sup>46</sup> Dreyfuss,<sup>47</sup> Nadoleczny,<sup>48</sup> Davis,<sup>49</sup> Ivy,<sup>50</sup> Mosciskier<sup>51</sup> and Kindler<sup>52</sup>

25 Gutzmann, Hermann Berl klin Wchnschr **36** 813, 1899, Physiologie der Stimme und Sprache, Braunschweig, Vieweg, 1928, Von den verschiedenen Formen des Naesels, Halle, C Marhold, 1901

26 Gersuny, R Ztschr f Heilk **21** 199, 1900

27 Lannois, M Rev hebdomadaire de laryngologie, d'otologie et de rhinologie **21** 177, 1901

28 Chiari, Ottokar Die Krankheiten der Nase, Leipzig, F Deuticke, 1903, vol 2, p 202

29 Helleu, Maxime Le pronostic des urano-staphyloporrhies pour fissures congénitales, Thèse no 313, Paris, 1904

30 Philip Ann d mal de l'oreille, du larynx **30** 597, 1904

31 Rouvillois Rev hebdomadaire de laryngologie, d'otologie et de rhinologie **28** 753, 1908

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34 Foucou Rev med de la Suisse Rom **30** 649, 1910

35 Blair, V P Tr Surg & Gynec A **23** 479, 1911, Surg Gynec Obst **12** 289, 1912

36 Roberts, John B Internat Clin **4** 220, 1918, Pennsylvania M J, 1920-1921, p 64

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39 Peter, Karl Atlas der Entwicklung der Nase und des Gaumens beim Menschen mit Einschluss der Entwicklungsstörungen, Jena, Gustav Fischer, 1913, p 112

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41 Stern, Hugo Monatschr f Ohrenh u Laryngo-Rhinol **53** 577, 1919, **54** 255, 1920, Arch f Laryngol u Rhinol **34** 95, 1921

42 Imhofer, R Ztschr f ang Anat u Konstitutionslehre **5** 146, 1920

43 Franke, Gustav Ueber Wachstum und Verildungen des Kiefers und der Nasenscheidewand, Leipzig, Kabitzsch, 1921, p 68

44 Bumba, Josef Monatschr f Ohrenh u Laryngo-Rhinol **56** 225, 1922

45 Apert and Bigot Bull Soc de pediat **20** 28, 1922

46 Rabattu, J Rev de laryngologie, d'otologie et de rhinologie **44** 859, 1923

47 Dreyfuss Ztschr f Hals-, Nasen- u Ohrenh **12** 253, 1925

48 Nadoleczny, Max Kurzes Lehrbuch der Sprach- und Stimmheilkunde mit besonderer Berücksichtigung des Kindesalters, Leipzig, F C W Vogel, 1926, p 71

49 Davis, Warren B Ann Surg **87** 536 (April) 1928

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51 Mosciskier, E Wien med Wchnschr **78** 961, 1928

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## VARIETIES

Congenital insufficiency of the palate may vary in accordance with the following forms

1 Cases in which the entire palate is normal in appearance, but in which the velum is unable to approximate the pharyngeal wall because of anteroposterior shortening of the hard palate and the velum

2 Cases in which the velum is normal in length and in which the hard palate is short

3 Cases in which the hard palate is normal and the velum shorter than normal

4 Cases in which the hard palate is normal in length and outline but in which there is a submucous cleft of the velum

5 Cases in which the velum is normal in appearance and length and in which there is a submucous cleft extending into the hard palate

6 Cases of insufficiency of the palate which occur after successful cleft palate operations, the velum being too short to reach the posterior pharyngeal wall

## ETIOLOGY

At the present time, the etiology of congenital insufficiency of the palate is unknown. The same conditions which cause other types of cleft palate, namely, an arrest in development due to some abnormal disturbance,<sup>53</sup> may result in congenital insufficiency. Just what the factors are that produce these deviations, one cannot say. It is known that heredity plays an important rôle, for defects may be handed down from generation to generation. Any type of defect may repeat itself in the offspring, and it is well known that persons with congenital anomalies of the palate frequently present malformations in other parts of the body. It is interesting to note the explanation offered for congenital deformities of the palate.

Fortunus Licetus,<sup>54</sup> in his writings published in the early part of the 17th century, recorded the accepted opinions of his time, regarding many of them as absurd. Among these were some of the widely prevalent Aristotelian views. Licetus attributed these anomalies to diseases of the fetus, maternal impressions, superfecundation and nutritional disturbances affecting the developing fetus.

Pierre Sylvian Regis,<sup>54</sup> in 1690, first called attention to the important rôle played by heredity in predisposing the transmission of these deformities. His views were supported by Winslow, Haller, Meckel and others.

Geoffrey St. Hilaire<sup>55</sup> proposed that mechanical influences were the main factors that produced these anomalies. Panum and Drete

<sup>53</sup> Rokitsansky, Carl. A Manual of Pathological Anatomy, Philadelphia, 1855, vol 2, p 17.

<sup>54</sup> Quoted by Tirifahy, S. J. de med. e chir. et de pharmacol. **37** 335 and 422, 1863.

<sup>55</sup> Quoted by Kramer, Josephy. Ueber Wolfsrachen und frühzeitige Urano-plastik, Inaug. Diss., Kiel, 1900.

attempted to support Hilane's views by experimentation Panum produced deformities in chickens by painting the eggs with varnish, and Dieste accomplished the same by placing the incubating eggs on one end

Violik and Nicati<sup>54</sup> also favored the mechanical theory, holding that the cleft palate was the result of increased development of the tongue which interposed between the palatal plates, preventing them from uniting in the midline His corroborated this theory and added that he felt that the upward pressure of the fist of the fetus on the mandible was instrumental in wedging the tongue between the palatal plates Panum later referred to the influence of amniotic adhesions in producing deformities of the palate

Ahlfeld<sup>56</sup> attempted to explain the presence of clefts by calling attention to the fact that hydrocephalus was a frequent factor in these cases He felt that the widening of the base of the anterior fossa of the skull in cases of hydrocephalus prevented the palatal plates from meeting in the midline Fern,<sup>54</sup> an ardent supporter of the mechanical theory, called attention to the presence of adenoids in cases of cleft palate, attributing their mechanical influence as a cause for the production of these deformities The association of adenoids with cleft palate or submucous cleft palate is certainly not a factor in producing the deformity, since adenoids do not appear in the fetus until the third month of intra-uterine life, a period at which the palate is completely formed

Warnekros,<sup>57</sup> demonstrating by means of the x-rays the presence of supernumerary teeth in cases of cleft palate, ascribed the latter to the presence of the former I feel that the presence of supernumerary teeth in cases of cleft palate is a mere incidence

Schorr<sup>58</sup> spoke of architectonic and vegetative factors which give rise to congenital deformities He pointed out that any interference with the process of mapping out the palate in definite directions favors vegetative growth, i e, growth in all directions, and that in these cases any degree of monstrosity may result

Grunberg<sup>38</sup> mentioned external and internal phenomena that act on the developing fetus He believed that malformations of the palate were largely due to internal disturbances which were within the developing fetus proper, including among these heredity

Bumba<sup>44</sup> suggested that syphilis was the chief internal factor involved Seeman<sup>12</sup> has dismissed this erroneous concept, obtaining negative Wassermann reactions in cases of submucous cleft palate

56 Ahlfeld Die Missbildung des Menschen, Leipzig, F W Grunov 1880

57 Warnekros Arch f Laryngol u Rhinol **21** 144, 1909

58 Schorr, George Virchows Arch f path Anat **197** 16, 1909

Charles Mayo<sup>59</sup> expressed his interpretation of anomalies in the following words:

As one observes birth defects or anomalies it is apparent that many of them are normal conditions in some lower form of life—e. g., harelip, cleft palate, fissure defects, anomalies in circulation, multiple ureters, dislocation of organs, clubfoot, postnatal dermoids and defects due to changes in the evolution of the intervertebrate to a vertebrate which largely affects the nervous system—encephalus, hydrocephalus, spina bifida. Experimentally, changes in the salts in which the eggs of several of the lower forms of life are developed lead to a certain percentage of monstrosities. This is undoubtedly the reason why a high type of fish like the salmon probably in an evolutionary state, leaves salt water

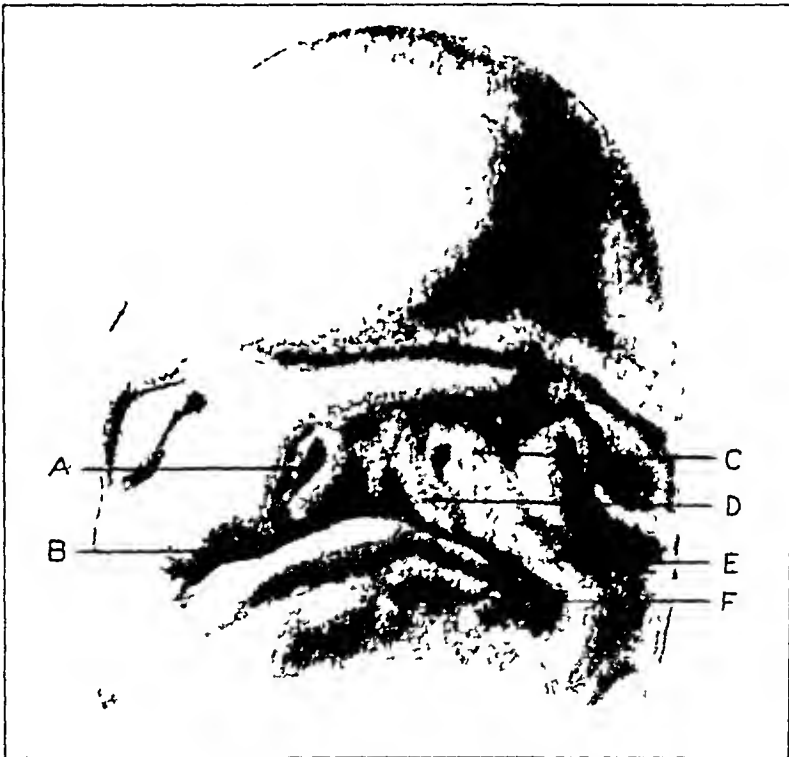


Fig 1—Head of a 15 mm human embryo,  $\times 18$  (After Peter) A indicates the anterior nares, B, stomodeum, C, lateral nasal process, D, globular process, E, maxillary process, F, mandibular arch

to lay eggs in fresh water. Anomalies in the embryo occur in variation in fluid, especially excessive quantity of hydramnion. It is most probable that the cause of embryonic deformities is due to the changes in the salts of the amniotic fluid in which the egg is developed, just as it happened to be in lower types of life.

As stated previously, despite the fascinating theories advanced in explanation of various anomalies, one is still unable to state definitely their etiology. Each form of anomaly of the mouth or of the palate

<sup>59</sup> Mayo, Charles. Discussion of Brophy's paper in *Tr. Sect. Surg., General & Abd., A. M. A.*, 1918, p. 30.

requires a separate embryologic interpretation. The following embryologic interpretation is limited to a consideration of submucous cleft palates alone.

The first branchial arches give rise to the maxillary processes which proceed forward to meet the descending nasofrontal process, the fusion of which forms the upper jaw (fig 1). From the mesial aspect of



Fig 2—Head of a 20 mm human embryo, from model,  $\times 13$  (After Peter)

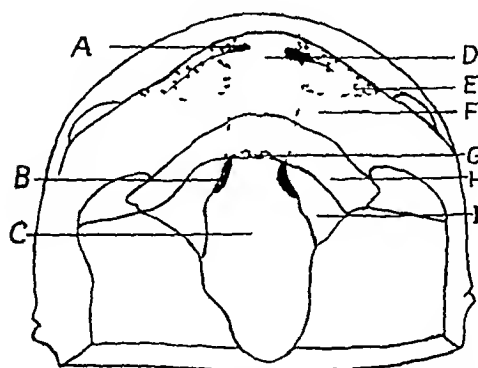


Fig 2 a—A diagrammatic sketch of figure 2. *A* indicates the anterior nares, *B*, primitive choana, *C*, roof of the primitive mouth cavity, *D*, middle nasal process, *E*, lateral nasal process, *F*, maxillary process, *G*, papilla palatina, *H*, alveolar process, *I*, palate process.

each maxillary process, ledge-like projections appear and advance toward the midline, where they unite with each other and the septum nares to form the involucrem palati (figs 2 and 3). An embryonal cleft palate or space lying between the palatal processes exists as a normal condition

in the embryo during the early stages of its development (fig 4 to be compared with fig 5) It gradually diminishes in extent as development progresses These processes begin to unite from before backward in the eighth week of intra-uterine life At the end of the ninth week, the hard palate becomes fully formed, although the velum remains cleft A few days later, however, the velum completely closes This fact, according to Grunberg,<sup>35</sup> explains the rarity of submucous cleft palate and the frequency of clefts involving the posterior part of the palate Evidently the disturbance of further union of the maxillary elements entering to form the involucrium palati sets in at the same time that union of the maxillary and nasofrontal processes begins anteriorly This primary union forms the primitive palate which separates the

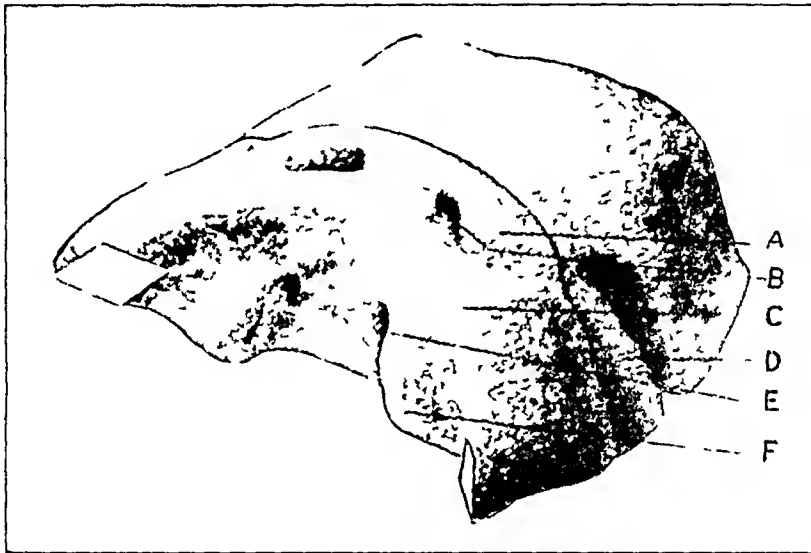


Fig 3—The anterior portion of the head of a 15 mm human embryo, from a model,  $\times 16$  (After Peter) A indicates the lateral nasal process, B, anterior nares, C, maxillary process, D, eye, E, primitive choana, F, palate ridge

anterior nares from the mouth cavity That part of the anlage which goes to form the oral mucosa continues its process of union and the soft tissue covering for the palate is thus formed to the tip of the uvula or perhaps to some distance anterior to it In the meantime, that part of the anlage which enters to form the bony palate and in which the process of union has been inhibited may or may not resume its function while the soft tissue anlage is in an advanced stage of development, in other words, the degree of submucous cleft palate is proportionate to the extent of inhibition of union in the mesodermic elements entering to form the bone This, according to Peter, explains the varieties of submucous cleft palate



Fig 4—Head of 30 mm human embryo,  $\times 10$  (After Peter)

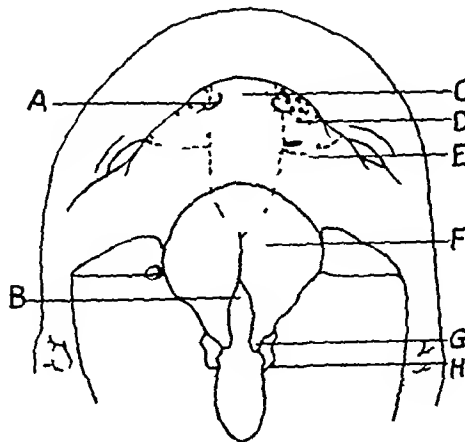


Fig 4 a—A diagrammatic sketch of figure 4 *A* indicates the anterior nares, *B*, cleft in the palate, *C*, middle nasal process, *D*, lateral nasal process, *E*, maxillary process, *F*, processus palatinus, *G*, uvula, *H*, palatopharyngeal fold

## APPLIED ANATOMY AND PATHOLOGY

The pharynx is suspended from the base of the skull by the fascia pharyngobasilaris, the attachment of which is shown in figure 6. To this fascia is attached the upper border of the superior constrictor muscle of the pharynx as shown in figures 7 and 8. The pharynx is also held dorsally to the tissue lying on the ventral aspect of the vertebral column by fascial strands extending from the prevertebral fascia. The pharyngeal canal is a muscular tube which moves freely upward and downward while performing its functions. Velopharyngeal closure is accomplished by a sphincter-like mechanism at the lowest part of the nasopharynx, which structure it shuts off from the oropharynx. This

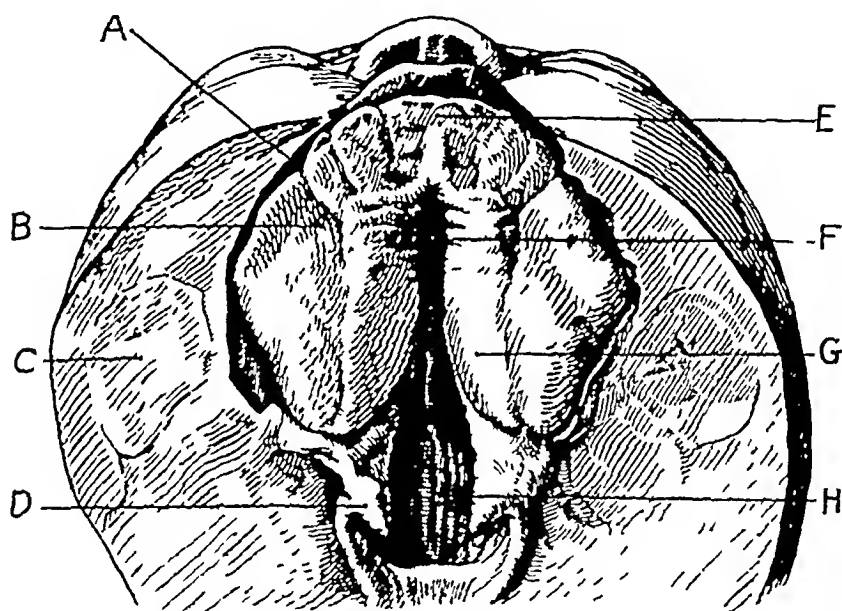


Fig 5—Cleft palate in a new-born child from Kollmann's Atlas (After Peter). *A* indicates the buccoalveolar sulcus, *B*, processus alveolaris, *C*, cheek, *D*, cleft in uvula, *E*, premaxilla, *F*, septum nasi, *G*, processus palatinus, *H*, base of the cranium.

mechanism is fairly complicated. The structures concerned in causing the closure are the lowermost portions of the nasopharyngeal wall on one side and the velum on the other. The portion of the nasopharyngeal wall which enters into this mechanism is composed of the posterior wall of the nasopharynx, the lateral walls of the pharynx with the eustachian tubes and the salpingopharyngeus bands of the palatopharyngeus muscles. The posterior wall of the nasopharynx where nasopharyngeal closure occurs is formed by the pterygopharyngeal portion of the superior constrictor muscle, which on contraction constitutes what is usually referred to as Passavant's cushion (fig 7). The velum from the standpoint of



function is divided into two parts, an anterior horizontal portion made up essentially of muscular tissues and a posterior vertical portion which hangs down from the former. The latter segment is formed almost entirely by the uvula. At the junction of these two portions there is an interlacing of the palatal muscles. It is at this point that the levator muscles are attached to the palatine aponeurosis. The levator palati muscle of one side blends with its fellow of the opposite side at their point of insertion into the palatine aponeurosis. So close is their union that the levator palati muscles must be considered as acting as one muscle. The backward and upward elevation of the velum depends

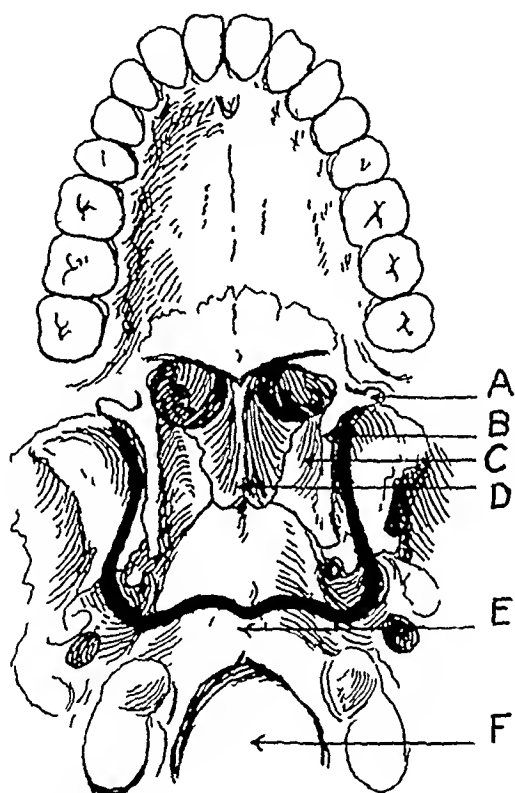


Fig 6—The heavy line shows the attachment of the fascia pharyngobasilaris to the base of the skull. *A* indicates the hamular process, *B*, pterygoid plate, *C*, sphenoid bone, *D*, vomer, *E*, occipital bone, *F*, foramen magnum.

exclusively on the position of the insertion of the levator palati muscles. Examination of figure 9 demonstrates this fact. The nasal aspect of this portion of the velum which corresponds with the attachment of the levator palati muscles approximates Passavant's cushion during velopharyngeal closure and forms the anterior segment of this mechanism. At rest, the uvula hangs down as a curtain, in ascending slightly on velopharyngeal closure, it contracts to make the vertical and dependent portion of the velum shorter. This causes the velal segment to become broader, thicker and shorter at the point of insertion of the levators (figs 9 and 10). The elevation of the pharynx brings these

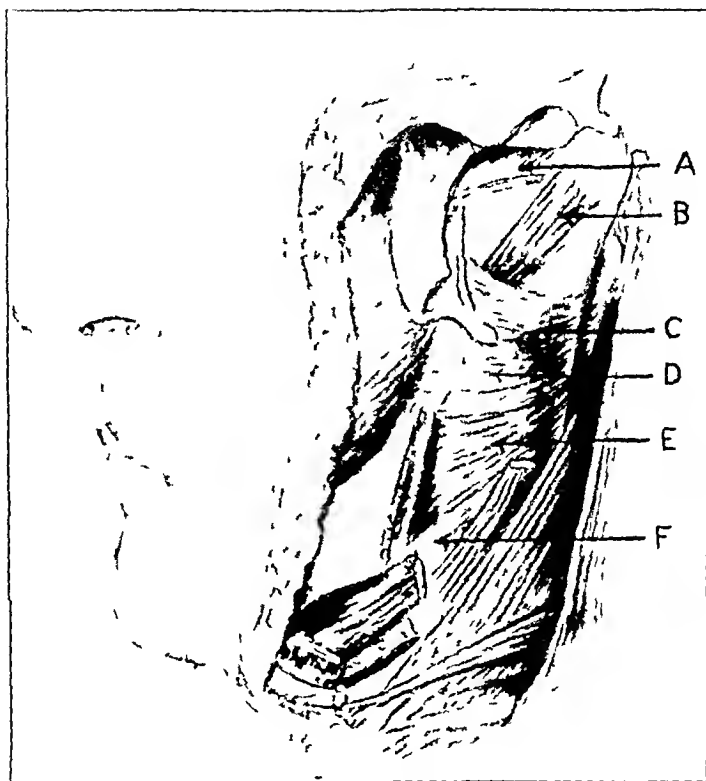


Fig 7—Lateral view of the pharynx, showing the superior constrictor muscle *A* indicates the tensor palati "cut", *B*, levator palati, *C*, pterygopharyngeus, *D*, buccopharyngeus, *E*, mylopharyngeus, *F*, glossopharyngeus

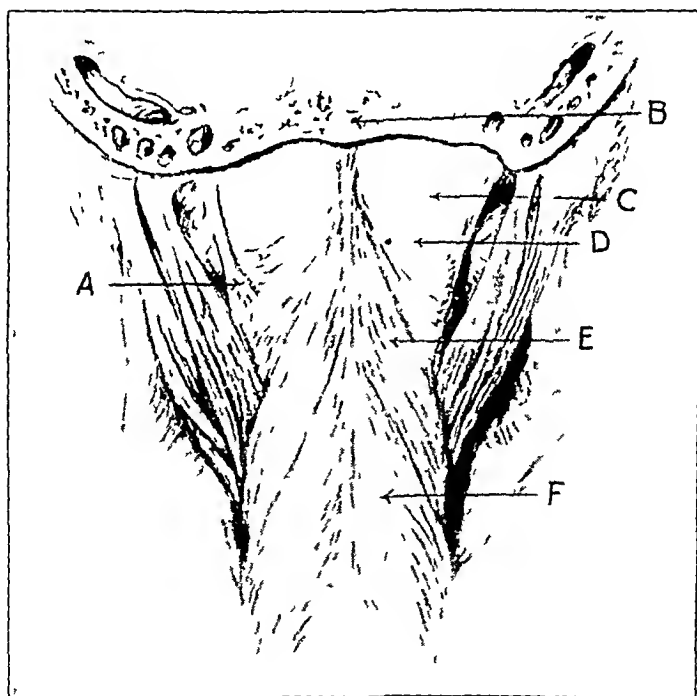


Fig 8—View of pharynx from behind *A* indicates the petropharyngeus muscle, *B*, occipital bone, *C*, fascia pharyngobasilaris, *D*, superior constrictor muscle, *E*, middle constrictor muscle, *F*, inferior constrictor muscle

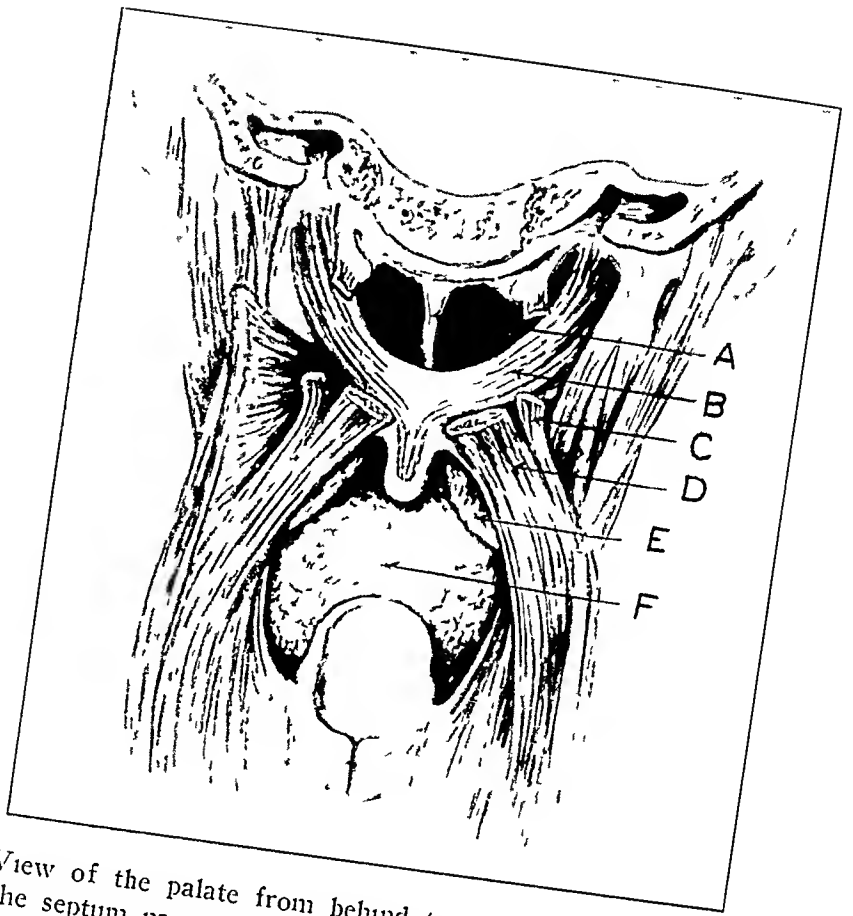


Fig 9—View of the palate from behind to show the levator palati muscles  
*A* indicates the septum nasi, *B*, levator palati, *C*, salpingopharyngeus "cut", *D*  
 palatopharyngeus "cut", *E*, faucial tonsil, *F*, dorsum linguae



Fig 10—Frozen sagittal section with the levator palati muscle dissected *A*  
 indicates the levator palati muscle

muscles into proper position enabling them to close the communication between the oral and the nasal portion of the pharynx. In other words, the superior constrictor muscle of the pharynx pulls the relaxed muscular tissue upward and forward while the lateral walls approach the midline. The velum is brought upward and backward by the contraction of the levator palati muscles. It is a well known fact that no muscle in the body acts alone without an antagonist to resist its action. It is also recognized that certain muscles in the body are so constructed that one portion of the muscle may exercise a certain function while another portion is moderately contracted or even at rest. The tensor palati muscles raise the velum up to the level of the hamular processes. Beyond this point they act as antagonists to the levators (figs 11a and

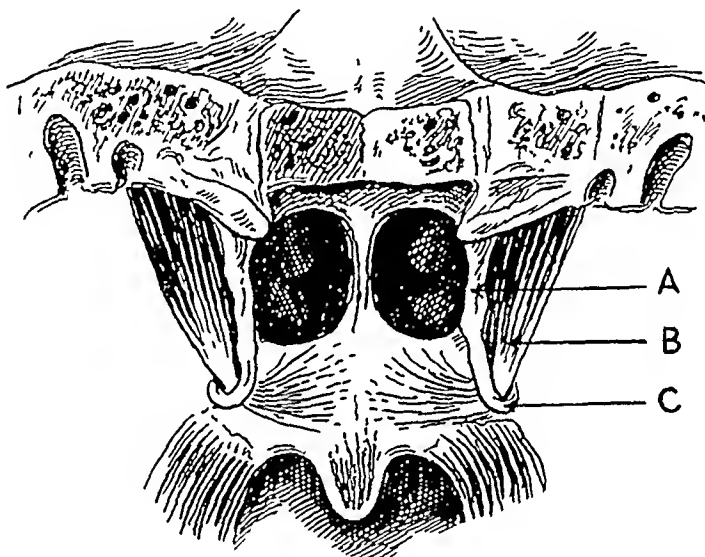


Fig 11 a—Sketch showing the tensor palati muscles. *A* indicates the mesial pterygoid plate, *B*, tensor palati muscle. *C*, hamular process.

11b) The tensor palati muscles make the palatine aponeurosis tense. Normally, the tensor palati muscles act together. The portion of the tensor palati muscles which arises from the eustachian tubes passes around the hamular process to be inserted into the horizontal plate of the palate bone in the transverse ridges. This portion of the muscle dilates the eustachian tube. The portion which arises from the scaphoid fossa at the base of the mesial pterygoid plate and the spina angularis of the sphenoid bone passes around the hamular process, radiating mesialward in a fan-shaped expansion to be inserted into the palatine aponeurosis and to interlace with its fellow from the opposite side. This portion of the muscle pulls the velum forward and outward, thus making the palatine aponeurosis tense. It is of interest to compare the function of this muscle in a normal palate with one in which a cleft

or submucous cleft is present. In the latter condition, the two tensor palati muscles act separately, thus pulling the velum forward and outward and at the same time turning the tips of the divided uvula inward toward the median line (figs 12, 13 and 14). Billroth<sup>60</sup> and Agnew<sup>61</sup> recognized this, and advised dividing the hamular process or the tendon of tensor palati muscles when attempting to close palatal defects.

To counteract the forward and outward pull of the tensor palati muscles in cases of cleft or submucous cleft palate, it is necessary to divide the posterior portion of the tendon of the tensor palati muscles. This portion of the muscle constitutes the lateral attachment of the palatine aponeurosis.

The palatopharyngeus muscle is difficult to dissect and more difficult to describe. The muscle has a portion known as the salpingopharyngeus



Fig 11 b—Photograph of specimen from the Mutter Museum of the College of Physicians of Philadelphia, showing dissection of the velum in man by Dr Adam Politzer. *A* indicates the levator palati, *B*, palatine aponeurosis, *C*, tensor palati, *D*, hamular process.

muscle which enters to form a muscular band in the lateral wall of the pharynx (figs 9 and 15). The other portion of this muscle constitutes the palatopharyngeus arch and runs from the velum downward to insert into the lateral wall of the pharynx. The palatopharyngeus muscle, on contracting, depresses the velum, thus acting as a direct antagonist to the levator palati muscles. This muscle, with its fellow of the opposite side, helps form the posterior pillars of the fauces. It is convenient to consider these pillars as a pair of muscles which act

<sup>60</sup> Billroth, Theodor. *Wien klin Wchnschr* **11** 241, 1889.

<sup>61</sup> Agnew, D. Hayes. *The Principle and Practice of Surgery*, Philadelphia, J. B. Lippincott Company, 1889, vol 2, p 974.

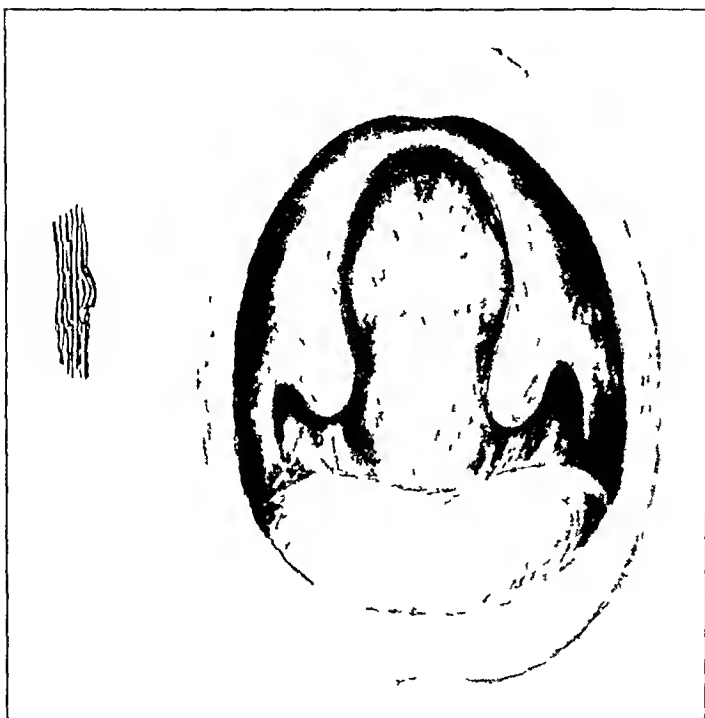


Fig 12—View of a case of cleft of the velum showing a well marked Passavant cushion

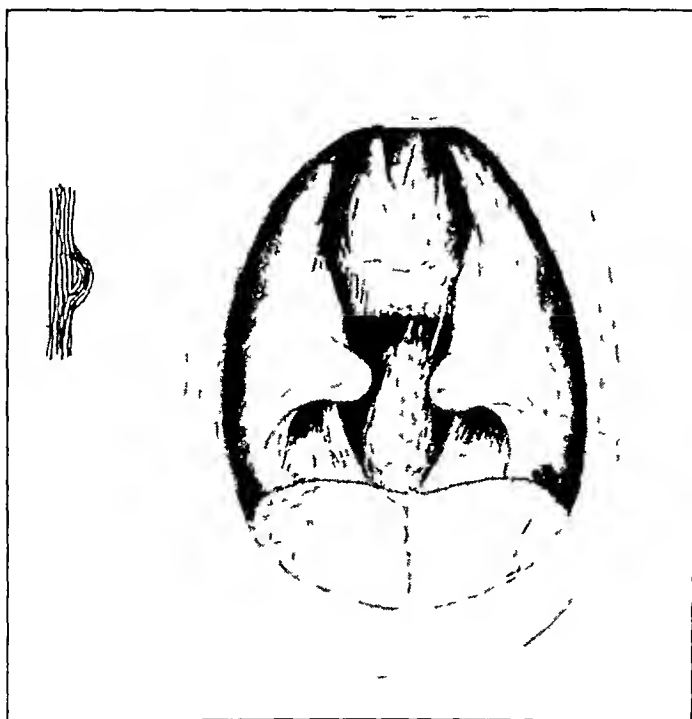


Fig 13—View of case shown in figure 12 while the patient attempts to contract the muscles slightly

synchronously. Their function has more to do with deglutition and vomiting than with speech, although they do draw the velum downward. Further details of their function are omitted since they do not enter into the velopharyngeal closure.

In cases of submucous cleft palate there is a deficiency in the posterior part of the bony palate (figs 16, 17 and 18). This deficiency may vary from a mere notch to a large V-shaped loss of bone. The palatine mucosa is always intact. The velum in this case is pulled forward with marked shortening in the anteroposterior diameter of the

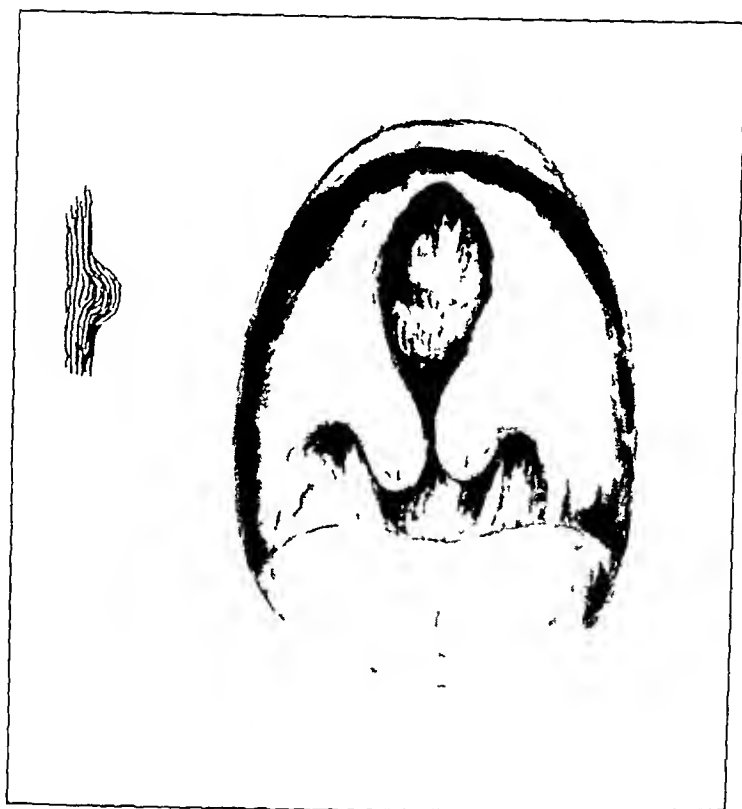


Fig 14.—View of case shown in figure 13 while the patient attempts complete contraction. Note how the sides of the cleft in the uvula approximate.

palate. The central portion of the velum which covers the deficiency in the bony palate is composed essentially of mucous membrane. This membrane can be seen to move up and down in the roof of the mouth during respiration. The insertion of the levator palati muscles in these cases is displaced forward. Hence they are unable to raise the velum upward and backward to the desired point against Passavant's cushion, at which point, as previously stated, velopharyngeal closure takes place. It must be remembered that there are cases of submucous cleft palate in which there is no loss of bone but a submucous cleft in the muscular tissues and in the palatine aponeurosis which enters to form the velum.

The superior constrictor muscle of the pharynx is composed of the pterygopharyngeus buccopharyngeus and mylopharyngeus muscles (figs 7 and 8). This muscle has other accessory muscular slips,<sup>62</sup> among which are the following petriopharyngeus sphenopharyngeus petropharyngeus externus, occipitopharyngeus mastopharyngeus and azygopharyngeus. These accessory muscular strands when present assist the superior constrictor muscle to elevate the pharynx. However, one or more are frequently missing. These muscles take their origin from the parts after which they are named.

The pterygopharyngeus portion arises from the pharyngeal raphe (fig 7). Starting about 1.25 cm to 2 cm below the pharyngeal tubercle

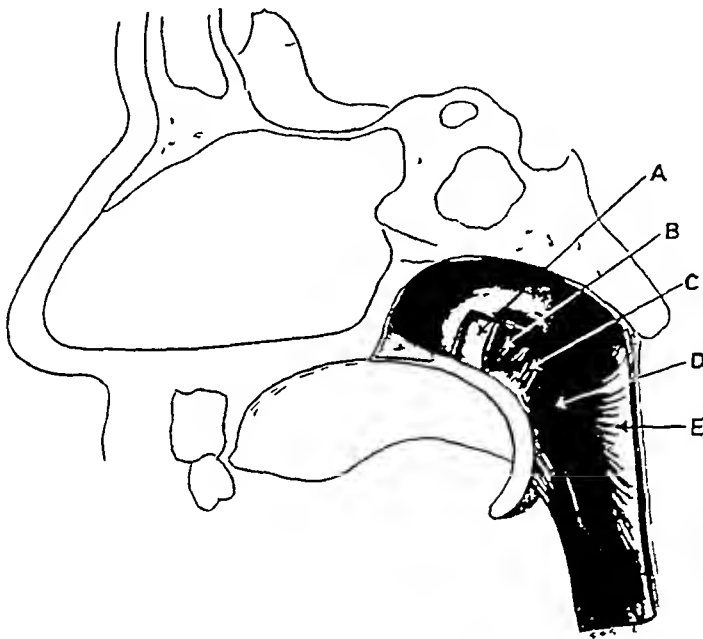


Fig 15—Dissection of the nasopharynx in cleft palate. *A* indicates the internal pterygoid plate, *B*, tensor palati, *C*, levator palati, *D*, salpingopharyngeus, *E*, superior constrictor. (From Wardill)

of the occipital bone, it runs outward and forward to the posterior border of the mesial pterygoid plate and hamular process. This muscle, which is the upper fasciculi of the superior constrictor muscle of the pharynx, forms Passavant's cushion.

The buccopharyngeus, which forms the lateral wall of the pharynx (fig 7), arises from the pharyngeal raphe and runs outward and upward to the pterygomandibular ligament. Its action produces a slight mesial constriction of the transverse axis of the pharynx.

<sup>62</sup> Toldt, Carl. *An Atlas of Human Anatomy for Students and Physicians*, tr. by M. Eden Paul, New York, The Macmillan Company, 1926.



The mylopharyngeus muscle arises from the pharyngeal raphe. It runs downward, outward and forward to the posterior one fifth of the mylohyoid ridge on the mandible. This muscle has nothing to do with velopharyngeal closure.

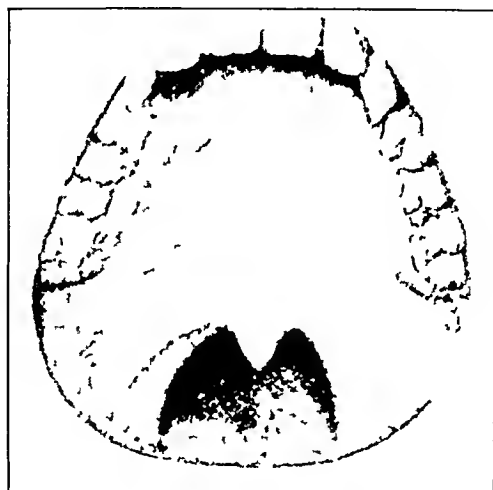


Fig 16—Submucous cleft palate (After A. Brown Kelly)

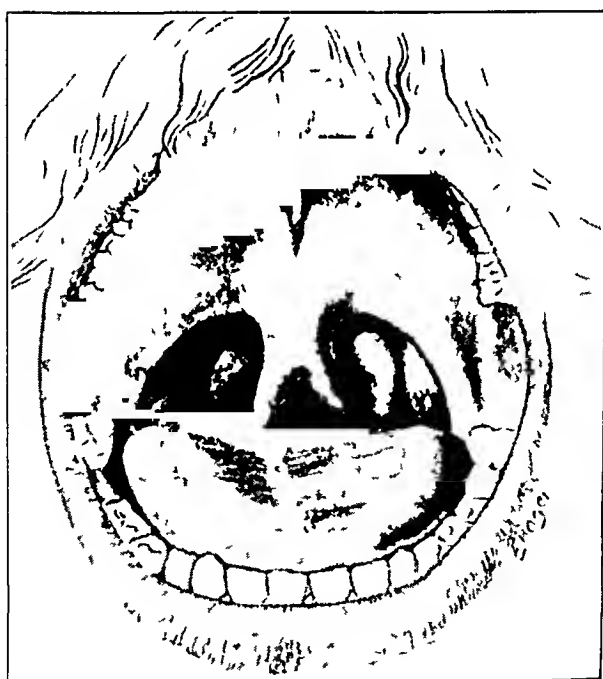


Fig 17—Submucous cleft palate with split of the uvula in a man, aged 40 (After Karl Peter)

The glossopharyngeus portion arises from the pharyngeal raphe, runs obliquely downward, outward and forward and inserts along the sides of the tongue, blended with the transverse linguae muscle.

My conclusions on the function of the pharynx were derived from dissections of human specimens, observations on normal and abnormal palatal cases and experimentations on animals. I believe that the pharyngeal muscles have varied actions, depending on the degree of the elevation of the pharynx. One can readily understand that if the pharyngeal raphe is tense, these muscles will pull in on either side, producing lateral narrowing of the pharynx, since they bring the lateral

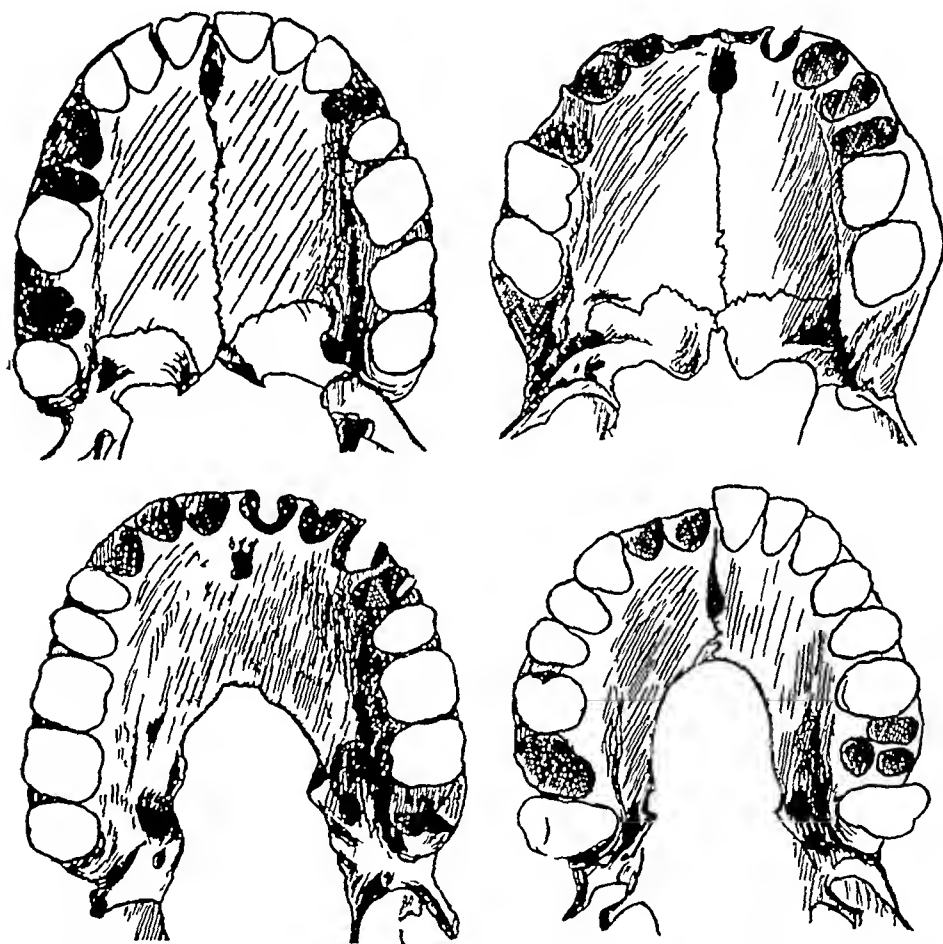


Fig 18—Sketches showing the varieties of missing portions from the posterior part of the hard palate (From A Brown Kelly)

walls toward the mesial line. When the entire pharynx is elevated through the action of the suprahyoid muscles the pharyngeal raphe is relaxed. Now contraction of the pterygopharyngeus muscles produces a condition as shown in figure 19. Without the assistance of the elevator muscles of the pharynx, the forward pull of the pharyngeal wall cannot take place, because the weight of the pharynx would prevent the weaker muscles from drawing it forward. As a matter of fact, when the superior constrictor muscle of the pharynx is observed

in a normal case it can be seen to contract by rolling forward and upward in a wavelike fashion, producing a ridgelike bulging

Until very recently, the walls of the pharynx have not been given sufficient consideration. When one observes velopharyngeal closure through the pharyngoscope or on persons who have suffered the loss of the nose and septum nasi, the nasopharynx has a close resemblance to a funnel the apex of which is directed downward. As closure occurs, the walls of the pharynx are pulled forward and inward by the superior

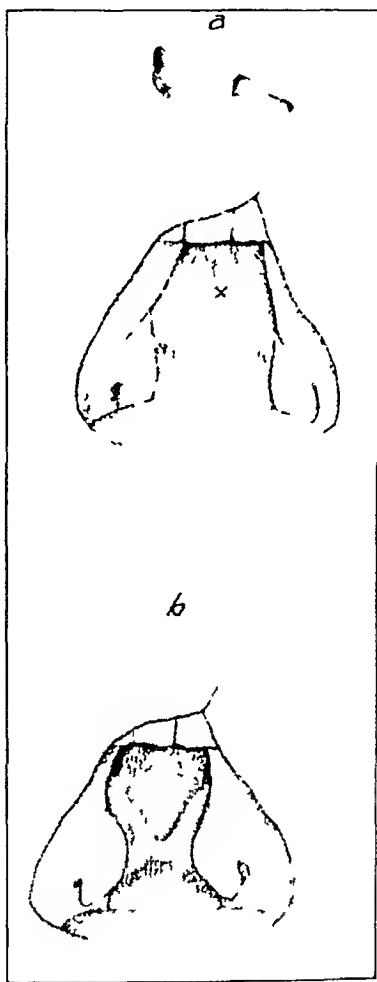


Fig. 19—In *a*, *X* shows Passavant's cushion at rest in a case of cleft palate. In *b*, the increase in size of the cushion is shown when "ah" is pronounced. (Taken from Passavant.)

constrictor muscles. The longitudinal bands formed by the salpingopharyngeus muscles contract, thus increasing the bulk and thickness of the wall and narrowing the lumen. The anterior segment is drawn upward and backward by the levator palati muscles. In persons with exceptionally well developed velopharyngeal closure the salpingopharyngeus muscle stands out like a band of muscular tissue which extends

from the mesial aspect of the eustachian cartilage, outward on the lateral wall of the pharynx, where it blends with the palatopharyngeus muscle. This muscle has two functions, either of which may be performed independently. That is, it may close the eustachian tube in the one case or may assist in the elevation of the pharynx in the other. Persons with palates which are normal in length can close the nasopharynx with but slight bulging of Passavant's cushion (fig 20). In persons whose palates are shorter than normal, velopharyngeal closure can be produced only by more active contraction of that portion of the pharyngeal wall which constitutes Passavant's cushion. It is remarkable how much development may occur in the pterygopharyngeus muscle following successful cleft palate operation or in cases in which the velum is stiff and insufficient. Likewise, the superior constrictor muscle of the pharynx can be forced to undergo marked development by continuous use.

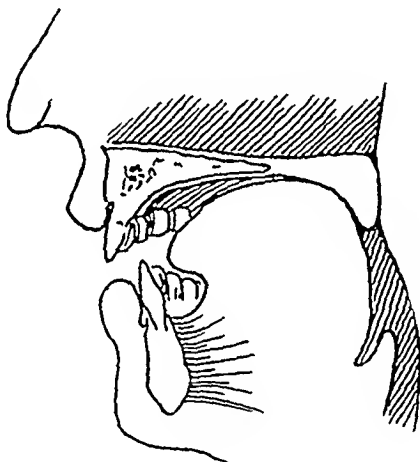


Fig 20—Sketch showing how normal velopharyngeal closure occurs. Note the forward movement of the posterior pharyngeal wall manifest by bulging of Passavant's cushion. The vertical portion of the velum is shown to assist in the sphincteric closure.

Velopharyngeal closure is complete in normal persons during the acts of swallowing, gargling and whistling or in the pronunciation of certain letter sounds which are free from nasal intonations. A simple test to determine whether the velopharyngeal closure is complete may be made by holding a cold mirror in front of the anterior nares while the patient forms the letter sound "ah", if closure is complete the mirror will be unclouded.

The palate has a copious blood supply derived from the nasopalatine vessels, the posterior and accessory palatine vessels and branches from the pharyngeal anastomosis. The nasopalatine arteries emerge from the anterior palatine foramen and anastomose with the posterior palatine

arteries The descending palatine arteries leave the greater palatine foramina and pursue a tortuous course within the palatine mucoperiosteum, supplying the hard palate, the alveolar processes and the gum tissues The branches which supply the hard palate anastomose freely with each other, but not with those of the opposite side The accessory palatine arteries leave the accessory palatine foramina and pass backward to anastomose with the terminal branches of the pharyngeal anastomosis They supply the velum The pharyngeal anastomosis is formed by the terminal branches of the lingual, facial and ascending pharyngeal arteries

The bony palate is said to have an independent blood supply,<sup>63</sup> and is thus protected from necrosis following cleft palate operations Following ligations of one or both external carotid arteries, collateral circulation is quickly established sufficient to nourish the tissues

Division of one or both posterior palatine arteries is frequently done in palatal operation Collateral circulation immediately takes care of the blood supply It is possible to divide the anterior and posterior palatine arteries in doing the "push-back operation" with perfect safety to the life of the flap, providing that an interval of one week is allowed to elapse before the second stage of the operation is done There are fewer mucous glands in the palate of children than in adults This explains the delicacy of the palatine mucoperiosteum in children and its inability to withstand surgical insult

The nerve supply of the palatoglossus, palatopharyngeus, salpingopharyngeus, azygos uvulae and the superior constrictor pharyngeus muscles is derived from the pharyngeal plexus This plexus is formed by branches from the glossopharyngeal, spinal accessory and pneumogastric nerves The tensor palati muscle<sup>64</sup> is supplied by the mandibular branch of the trigeminus The levator palati<sup>64</sup> is supplied by the bulbar root of the spinal accessory nerve, which contains the inferior rootlets of the pneumogastric nerve

#### DIAGNOSIS AND SYMPTOMS

The diagnosis of congenital shortening of the palate can be accurately determined only after the child makes efforts to speak On examining children before the age of speech, one may observe that the velum is unable to approximate the pharyngeal wall to secure the desired velopharyngeal closure The final diagnosis cannot be definitely established until a considerable period of time after the child develops articulate speech Children with congenital shortening of the palate usually learn to speak at a later period than normal children These children speak

63 Berry James and Legg, T Percv Harelip and Cleft Palate, Philadelphia, P Blakiston's Son & Company, 1912, p 34

64 Rich A R Bull Johns Hopkins Hosp 31 307, 1920

very indistinctly, owing to the inability of the velum to approximate the pharyngeal wall to produce the desired velopharyngeal closure. It is true that as these children develop and make persistent efforts to speak, their speech becomes more and more distinct, depending on their ability to develop a mechanism to compensate for this velopharyngeal insufficiency. They develop the compressor naris muscles and a hypertrophy of the muscles which produce the velopharyngeal closure and they frequently develop a hypertrophy of the faucial and pharyngeal tonsils.

The diagnosis is made from the following symptoms

- 1 Rhinolalia aperta or open nasalizing. This begins at the period when the subject began to talk. The vowels take a nasal tone, i. e., the letter "a" becomes "an," etc. The consonants become very much altered, with the exception of the letters "m" and "n" which retain their characteristic sounds. Sigmatisms or the inability to produce the letter sound "s" becomes very pronounced in these cases.

- 2 These patients suffer from shortness of breath in speaking due to the loss of air through the nose.

- 3 They are unable to whistle.

- 4 Hissing becomes impossible.

- 5 Patients are unable to blow out a candle flame from a distance, unless they have developed a method of compressing the nares.

- 6 Breathing by mouth becomes a habit, giving these patients a characteristic vacant expression.

- 7 Movements of the facial muscles, more especially the compressor naris and the corrugator superciliary muscles, become pronounced. These patients are referred to as "face talkers."

- 8 Hearing may be diminished, owing to improper ventilation of the middle ear. Nasal catarrh is frequently present.

- 9 Deglutition may become disturbed in children. When these patients become older, they may have difficulty in swallowing.

- 10 These patients talk very rapidly, and avoid difficult words.

- 11 Intra-oral examination reveals a distinct velopharyngeal insufficiency. The patient is unable to shut off the nasopharynx from the oropharynx because of the anteroposterior shortening of the palate. Here the shortening may be the result of a shortened hard palate or a shortened velum, or both. The superior constrictor muscle of the pharynx may be weak.

- 12 Intranasal examination by the pharyngoscope reveals an insufficient velum, which is unable to shut off the nasopharynx.

- 13 The uvula is bifid in some cases.

- 14 Palpation may reveal a submucous cleft of the hard palate, this may vary from a mere notch to a considerable V-shaped deficiency in the median portion of the bony palate (fig 18). The palatine mucosa is found intact. The submucous cleft may involve the velum alone, the hard palate being intact.

- 15 Irregularity and crowding of the teeth, or congenital absence of the second maxillary incisor tooth, or the association of cleft lip, or the evidence of an intra-uterine healed cleft of the velum may be present.

The palate varies in length with the age, sex, race, build and general characteristics of the individual. Not infrequently, a history of defects in speech or even a case or two of congenital anomalies in the forebears is disclosed on taking a careful family history. If the palate assisted by the superior constrictor muscle of the pharynx is unable to shut off the nasopharynx, it must be considered a short palate. While complete velopharyngeal closure is essential for normal function, this mechanism is not always hermetically sealed during speech, since a certain amount of air escapes through the nostril as certain letter sounds are produced. It is interesting to mention here that Schmidt<sup>65</sup> determined by experiments that speech could remain normal while there was a rubber tube with a lumen of 6 mm. between the velum and the pharyngeal wall, but when a tube of a larger lumen was inserted speech became nasal. This shows that the superior constrictor muscle of the pharynx is capable of overcoming a certain amount of insufficiency which if increased beyond 6 mm. cannot be overcome by this muscle. The shortness of the palate determines the degree of insufficiency. The most reliable test is to hold a piece of cotton in front of the anterior nares while the patient makes efforts to pronounce non-nasal letter sounds. The escaping air makes the cotton move when this mechanism is insufficient. In diagnosing congenital insufficiency of the palate, the condition should not be confused with palsy of the velum, stomatolalia and speech defects, the result of loss of the teeth or in faulty lingual articulation observed in some cases after successful cleft palate operation. In all of these cases, the velopharyngeal closure is normal.

Palsy of the palate is easily recognized by the absence of the palatal reflex, the inability of the velum to move and its lack of response to faradic stimulation.

Stomatolalia or so-called "rhinolalia clausa" is a condition of speech in which the letter sounds lack their necessary nasal resonance, a quality of the speaking voice which determines the supreme elegance of a spoken language.

Defects of speech, the result of the loss of teeth and faulty habits in the use of the tongue, are easily recognized. Loss of the teeth can easily be restored by dentures. Faulty habit in using the tongue can be corrected with methodic speech training.

#### TREATMENT

In reviewing the literature, one is constantly impressed by the fact that the early pioneers in the field of palatal surgery recognized that perfect speech could be obtained only when the velum was brought in contact with the posterior wall of the pharynx. Many ingenious methods

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65 Quoted by Gutzmann (footnote 20)

were devised to accomplish this. One group exerted their efforts to lengthening the palate, another group sought to bring the wall of the pharynx forward, while a third group advised the use of artificial vela. Even today, many surgeons, after failing to obtain a good functional result when the repair was surgically perfect, advise dividing the sutured velum so as to permit the insertion of an artificial velum. The artificial vela of Suesen, or Kingsley, or any modifications of these vela are generally employed. These vela are constructed from soft or hard vulcanite, the latter being the most serviceable. Whenever appliances are instituted for treating insufficiency of the palate, the patient should be informed of the necessity of renewing them from time to time. Through continuous use and due to the fact that the palatal muscles and the superior constrictor muscle of the pharynx hypertrophy, such contrivances lose their relationship with the surrounding structures and new appliances become necessary in order to obtain proper velopharyngeal closure. Obturator-vela may be indicated occasionally in adults, but are rarely necessary in children unless the condition warrants no other method of treatment.

Passavant's<sup>3</sup> observations on speech after successful closure of the cleft palate led him to ascribe nasal intonation in these cases to the inability of the velum to approach the pharyngeal wall. In 1862, he suggested partial union of the velum with the pharyngeal wall to obtain the proper closure. He advised the introduction of sutures on either side of the freshened palatopharyngeus muscles and to a corresponding area on the posterior wall of the pharynx. Passavant also mentioned that union of the palatopharyngeus muscles for a certain extent in the midline may be combined with staphylorhaphy. However, in 1865, he outlined three different operations to secure the necessary approximation.

The first of these operations consisted in uniting the palatopharyngeus muscles for a certain distance in the midline so as to raise the posterior portion of the velum and so displace it backward to approximate the pharyngeal wall. The upper portions of the mesial border of the posterior pillars were freshened and united by suture after the lateral incisions were made into the velum (fig. 21). This union was obtained in three cases for the distance of 1.25, 2 and 2.5 cm., respectively. Speech was only slightly improved in these cases, nasal intonation persisting.

The second operation which he called staphylopharyngorrhaphy consisted of producing velopharyngeal adhesion. Passavant made a transverse incision across the velum, through this incision, he introduced a spatula bent on the flat. This enabled him to evert the velum permitting its free border to be directed forward. The velum was freshened on its free border for a distance of eight lines in length and five lines in depth.



a corresponding area on the pharyngeal wall was then freshened at the point where velopharyngeal closure was desired. The free border of the velum was then approximated to the posterior wall of the pharynx and sutured (fig 22). This procedure, as pointed out by Passavant, gave better results than his former method.

Staphylopharyngorhaphy as suggested by Passavant must be condemned. Though its use stomatolalia is established, normal ventilation of the eustachian tubes is interfered with, and the accumulation of mucous secretions in the nasopharynx is favored.

The third operation consisted of making lateral incisions 1 inch long on either side, mesial to the hamular process, and running anteriorly parallel with the alveolar margin. The anterior extremities of

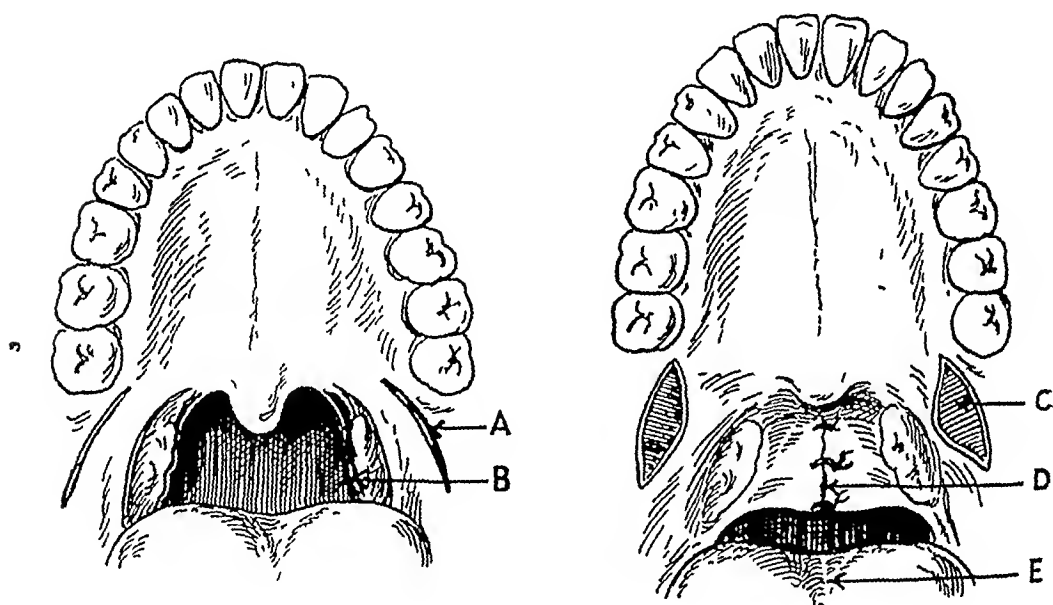


Fig 21—Artist's conception of Passavant's operation for suture of the palatopharyngeus muscles. *A* indicates the lateral incision, *B*, freshened border of the posterior pillar, *C*, area to close by granulations, *D*, line of sutures, *E*, dorsum linguae.

these two incisions were joined with a third incision running transversely across the palatine mucoperiosteum. The quadrilateral flap inscribed by these three incisions with its base directed posteriorly, in continuity with the velum, was freed from the underlying bone (fig 23). The entire velum was displaced backward, and held by suture to the posterior pharyngeal wall. At a subsequent operation, the defect in the hard palate was closed by some autoplasmic method. Passavant reported satisfactory results from this procedure.

Nevertheless, in 1878, he condemned all his previous operations and devised one for the correction of velopharyngeal insufficiency. He now proposed a procedure to obtain a bulging of the posterior pha-

ryngeal wall This was accomplished by inscribing a quadrilateral flap on the posterior wall of the pharynx mesial to and above the level of the eustachian tubes, with the base in connection with the mucous membrane, covering the superior constrictor muscle of the pharynx This flap was separated from the underlying tissue and folded over on the raw surface, being held in position by sutures (fig 24) A shelflike projection was thus made on the posterior wall of the pharynx The sides of this ridge were then united by suture to a corresponding area on the lateral walls of the pharynx The tissue covering the sphenoid bone which was used to fashion this projection was found to be inadequate for this purpose, as the shelf in time gradually disappeared

Finally, Passavant made use of an obturator modeled after the shape of a shirt stud (fig 25), thus he inserted into a button-hole incision

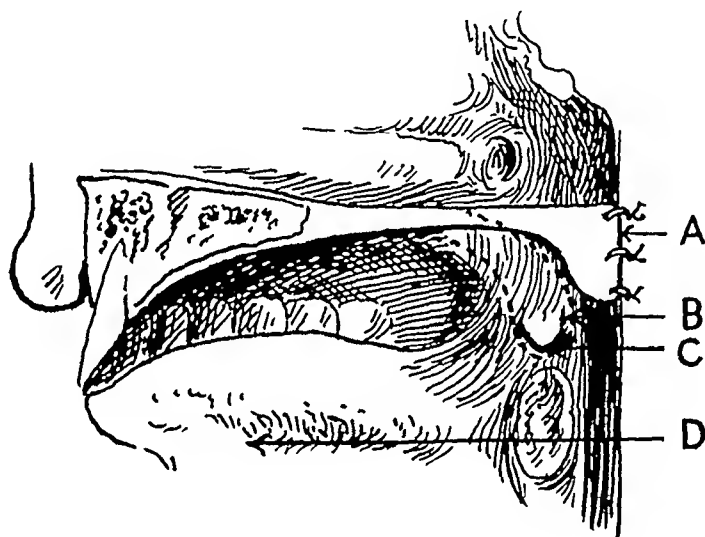


Fig 22—Artist's conception of Passavant's operation to produce staphylopharyngorrhaphy *A* indicates the velum and posterior pharyngeal wall sutured together, *B*, the dotted line to show position of velum, *C*, the heavy line to show free border of velum which has been freshened, *D*, the tongue

running transversely across the middle of the velum through its full thickness The purpose of this plan was to secure backward displacement of the soft palate and thereby to establish the desired closure

In 1864, Simon<sup>14</sup> suggested that the nasal speech which persists after successful cleft palate operations might be corrected by inserting gum balloons into the nostrils or by applying a pince-nez device on the alae nares so as to shut off the escaping air These methods proved to be inadequate, as the formation of the letter sounds lacked the proper nasal resonance

In 1867, Simon suggested the use of Dieffenbach's osteal uranoplasty to obviate velopharyngeal insufficiency His operation consisted of

freshening the edges of the cleft in the hard and soft palate, along with scarifying the edges of the bone. Lateral incisions were made on either side into the hard palate down to the bone at a distance varying from one and one-half to two lines from the alveolar margin. The mucoperiosteum surrounding these lateral incisions was then elevated from the underlying bone. The bony palate was sawed through at the site of the lateral incisions (fig 26), beginning behind at a point about one-half line mesial to the hamular process, thus dividing the palatal processes from their alveolar connection. The division through the bone was extended anteriorly as far forward as the termination of the lateral incisions. A lever was then introduced into these lateral incisions in the bone and the anterior attachment of the palatal processes were fractured to produce their mesial displacement. This supplied two

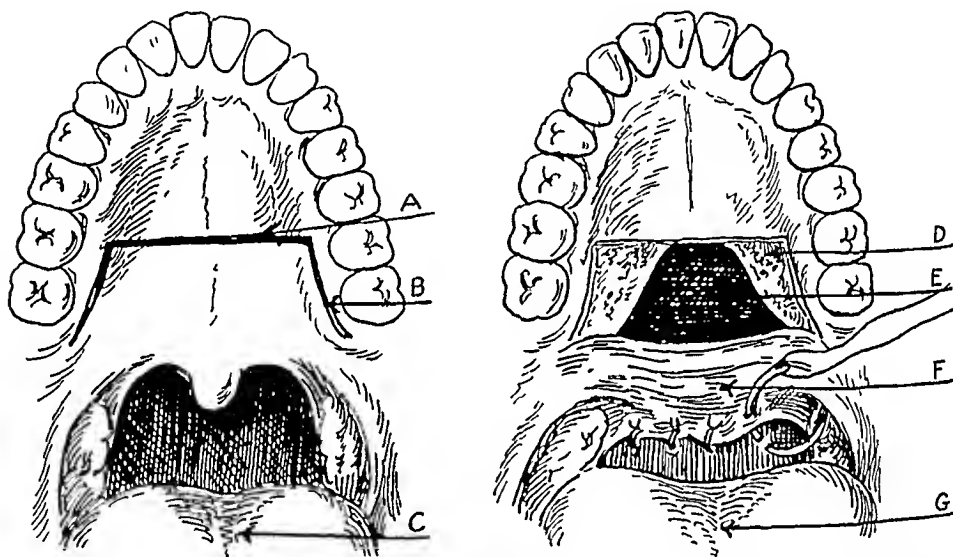


Fig 23—Artist's conception of Passavant's operation for backward displacement of the velum. A indicates the transverse incision, B, lateral incision, C, dorsum linguae, D, denuded bone, E, nasal cavity, F, displaced velum, G, dorsum linguae.

freely moving osteomucous flaps which were attached anteriorly to the palatine mucoperiosteum situated behind the incisor teeth, and posteriorly with the soft tissue in continuity with the velum. These flaps were then approximated toward the median line and united with sutures applied through the mucoperiosteum.

Osteal manoplasty was first suggested in 1826, by Dieffenbach,<sup>66</sup> and later by Wutzer<sup>67</sup> and Buhring<sup>68</sup> in 1850. In 1873, Fergusson<sup>69</sup>

66 Dieffenbach. *Litt Ann d ges Heilk* 4 145, 1826, *Die operative Chirurgie*, Leipzig, F A Bockhaus, 1845, vol 1, p 856.

67 Wutzer, C W. *Deutsche Klin* 2 26, 1850.

68 Buhring, Julius. *J d Chir u Augenh* 9 325, 1850, *Deutsche Klin* 2 472 1850.

69 Fergusson, Sir William. *Lancet* 2 784, 1873, 1 298 and 883, 1874.

modified this method. The operation, although formidable, was performed from time to time by different cleft palate surgeons on the European continent and in America, among whom Mears and Roe of Philadelphia are worthy of mention. Brown of Milwaukee and Davis<sup>40</sup> of Philadelphia have recently popularized osteal uranoplasty, using it as their method of choice in suitable cases of cleft palate.

Paul,<sup>70</sup> in 1866, advised broadening the stiffened and narrowed velum resulting from staphylorhaphy by making repeated lateral incisions in the velum. These heal by granulations. This method is based on the same principle of healing by granulations brought out by

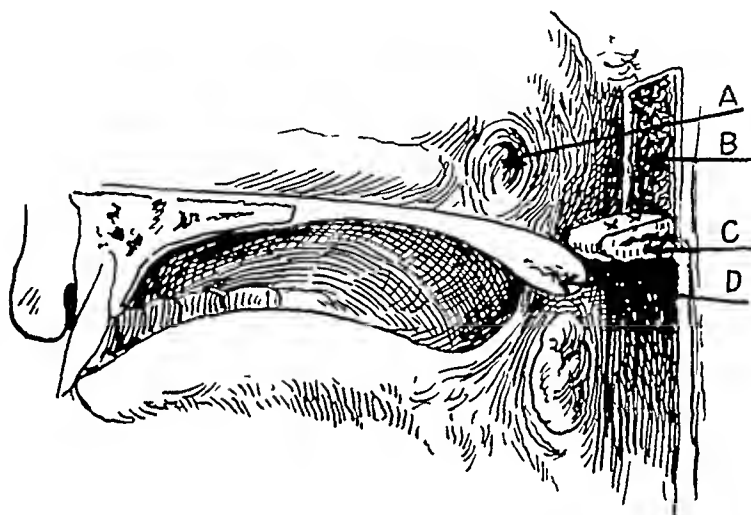


Fig 24—Artist's conception of Passavant's operation for making a shelflike projection on the posterior pharyngeal wall. A indicates the eustachian tube, B, denuded area, C, projection, D, velum.



Fig 25—Passavant's stud-shaped obturator (After Kuster)

Mettauer<sup>71</sup> of Virginia for performing staphylorhaphy (figs 27 and 28). The rationale of this method was that the granulations resultant from the healing of these wounds added bulk to the velum, producing an increase in the tissue and thus assisting velopharyngeal closure.

Mason,<sup>72</sup> in 1869, advised for correction of nasal speech after cleft palate operations otherwise successful the making of lateral incisions

<sup>70</sup> Paul, Hermann Julius. *Arch f klin Chir* 7 199, 1866.

<sup>71</sup> Mettauer, John B. *Am J M Sc* 21 331, 1837.

<sup>72</sup> Mason, Francis. *Lancet* 2 198, 1869, 2 578, 1874, *St Thomas Hosp Rep* 2 271, 1871, *On Cleft Palate and Harelip*, London J & A Churchill, 1877 p 114, *The Retrospect of Practical Medicine and Surgery*, 1870, p 123.

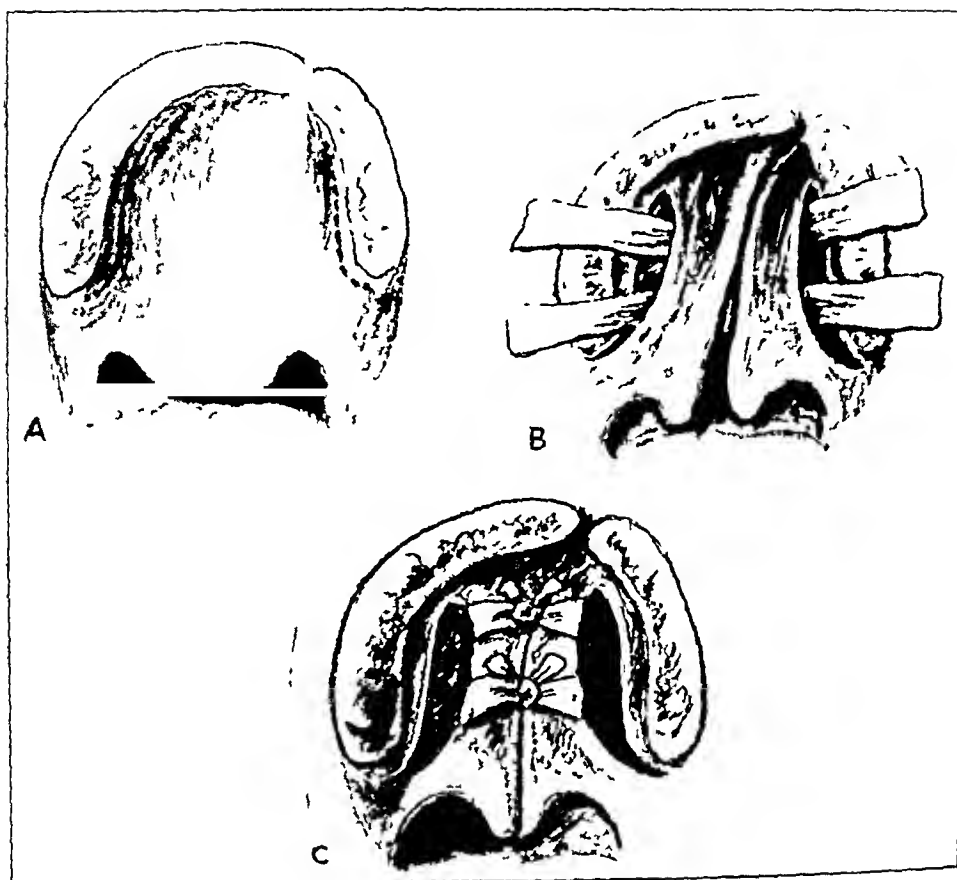


Fig 26—Steps in osteal uranoplasty (After Davis) *A* is a semidiagrammatic sketch showing unilateral cleft palate and the outline of incisions (slight extension of the Langenbeck incision) used in loosening the mucoperiosteal flap on the side attached to the vomer and loosening the flap containing the rudimentary horizontal process of the maxilla and of palate bone on the opposite side. The latter incision is carried through the periosteum after which the horizontal processes are cut through with a very thin chisel. *B* is a semidiagrammatic sketch showing a mucoperiosteal flap loosened on the patient's right side and a flap containing bone on the patient's left side. In the two-stage operation, tapes are passed around both flaps and tied so as to hold the medial margins of the flaps in apposition, or nearly so, care being taken not to exert sufficient pressure by the tapes to shut off circulation. Iodoform gauze packs are used in the lateral incisions for twenty-four hours. *C* is a semidiagrammatic sketch showing the tapes tied so as to hold the medial margins of the flaps in apposition. Iodoform gauze packs are used in the lateral incisions for twenty-four hours. One tape is removed on the third or fourth day, the remaining tape on the fifth or sixth day. On the seventh day, the mucous membrane is removed from the margins of the clefts and sutures applied.

into the full thickness of the velum internal to the hamular process, to run posteriorly through the free border of the velum. The result of such a procedure altered the stiffened velum into a large floating uvula which was unable to approximate the pharyngeal wall. Mason gives the following description of his operation:

A small curved spatula is first placed behind the soft palate, it keeps the part steady and also serves as a point d'appui. A sharp pointed knife is then introduced from before backward (*A* fig 29) in about the position of the inner edge

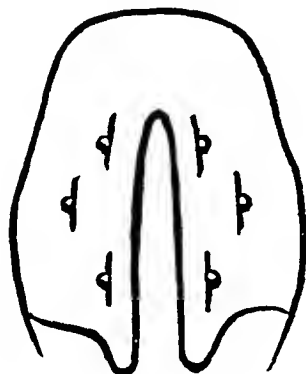


Fig 27—Mettauer's incisions to produce healing by granulations in clefts of the velum (From Mason)

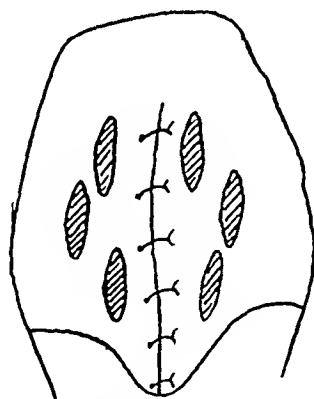


Fig 28—Diagrammatic sketch to show the velum after the application of sutures. The shaded areas to close by granulation tissue (Modified from Mason)

of the hamular process in the normal palate (*D*), and the soft palate is cut completely through from above downwards from *A* to *B*. The same is done on the opposite side, and the operation is then concluded. In the first few cases on which I operated, I hemmed the mucous membrane back and front as indicated in the diagram *E*, but I have long since abandoned this practice, as unnecessary for when the parts unite, they do so at the V-shaped angle where these are in immediate contact (dotted line *F*). The operation is quite simple and may be repeated as often as necessary, is perfectly free from danger, and almost painless. The rationale of the proceeding is easily explained. The palate becomes converted into a huge uvula so to speak. It is shortened and puckered up the

point *B* being drawn to *C* so that if it does not actually touch the back of the pharynx, it approaches so nearly as to divert the current of air to a considerable extent from the nose into the mouth and thus greatly obviates the disagreeable guttural voice that is more or less observable in all patients who are subjects of this distressing deformity

It is evident from Mason's description that his operation gave freedom to the palate because of the complete relaxation obtained by the division of the tensor palati muscles. The incisions used by him undoubtedly divided the opponents to the levator palati muscles and thereby enabled the velum to be more easily raised.

Whitehead<sup>73</sup> of New York, in 1871, attempted to lengthen the velum by adding to it two lateral flaps dissected from the posterior pillars of

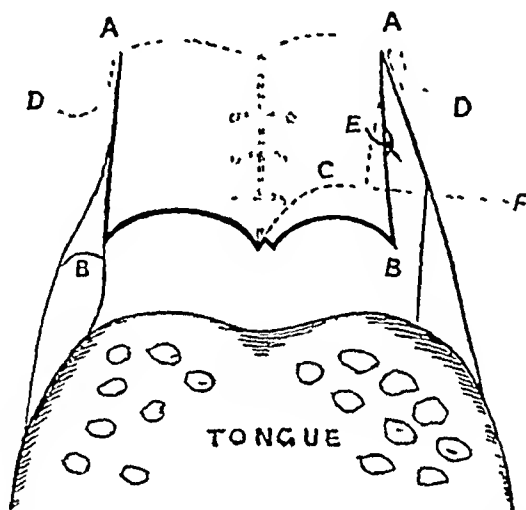


Fig. 29—Mason's operation for the improvement of speech after cleft palate operations (From Mason)

fauces and the lateral walls of the pharynx (fig. 30). He described his procedure in the following words:

About the first week of February, assisted by Dr. Henry Schiff of this city, I endeavored by a difficult and laborious dissection of the palatopharyngeus muscles, to form flaps with which to lengthen the velum palati. Having seized, with a pair of forceps, the palatopharyngeus on the right side very low down, I divided this muscle and a part of the mucous membrane of the prevertebral region, and dissected upward with a pair of curved scissors a flap more than sufficient to form, with a corresponding one on the opposite side, a long and dependent curtain to the new velum.

Makuen, of Philadelphia, has been mentioned by Brophy<sup>74</sup> (figs. 31 and 32) and others as having developed the method by which two

<sup>73</sup> Whitehead, William R. *Am J M Sc* 62:114, 1871.

<sup>74</sup> Brophy, Truman W. *Oral Surgery: A Treatise on Disease, Injuries and Malformations of the Mouth and Associated Parts*, Philadelphia, P. Blakiston's Son & Company, 1915, p. 709; *Cleft Lip and Cleft Palate*, Philadelphia, P. Blakiston's Son & Company, 1923, p. 252.

flaps are raised from the palatopharyngeus arch and sutured to the free freshened border of the velum. The works of Makuen<sup>75</sup> do not present this operation. The only remark he made on this subject was in 1901 when he mentioned separating the adhesions between the pillars of the fauces and remnants of the tonsils on either side to overcome velopharyngeal insufficiency. This use of the posterior pillars of the fauces proved to be of no value. It is interesting to mention here that in 1912, Helbing<sup>76</sup> used the posterior pillars to increase the size of the velum as is shown in figure 33. Helbing freshened the mesial border of the palatopharyngeus arch extending this denudation over the intervening portion of the free border of the velum. An incision was then made on either side dividing the posterior pillars as shown at *X*. Side incisions were also made within the velum to release all tension. The freshened edges of the palatopharyngeus arch were united in the midline by suture.

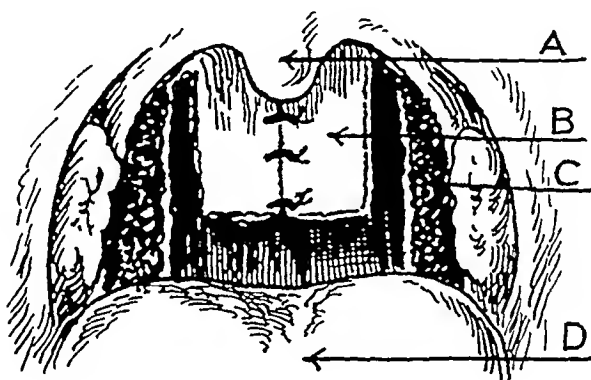


Fig 30—Artist's conception of Whitehead's operation, showing the use of the palatopharyngeus muscles in lengthening the velum. *A* indicates the uvula, *B*, posterior pillars sutured in midline, *C*, area to close by granulations, *D*, tongue.

Interference with the palatopharyngeus muscles changes the flexibility of these muscles so that they become more or less rigid, non-elastic bands of tissue which hold the velum downward and prevent it from being elevated beyond a certain point. The use of the posterior pillars in palatal operations is of no value in raising the velum and is a decided hindrance to its free movement during speech and deglutition.

As already pointed out in this paper in the section dealing with anatomy the uvula only slightly assists in closing the nasopharynx. Velopharyngeal closure is produced by the combined action of the levator palati muscles and the superior constrictor muscle of the pharynx. The

<sup>75</sup> Makuen, G. Hudson. *Am Med* 2:532, 1901.

<sup>76</sup> Helbing, Carl. *Berl klin Wchnschr* 49:980, 1912. *Allg med Centr Ztg* 81:21, 1912. *Die Technik der Uranoplastik*, im Pavy und Kuettner. *Ergebnisse der Chirurgie und Orthopädie*. Berlin, Julius Springer, 1913, vol 5, p 81.



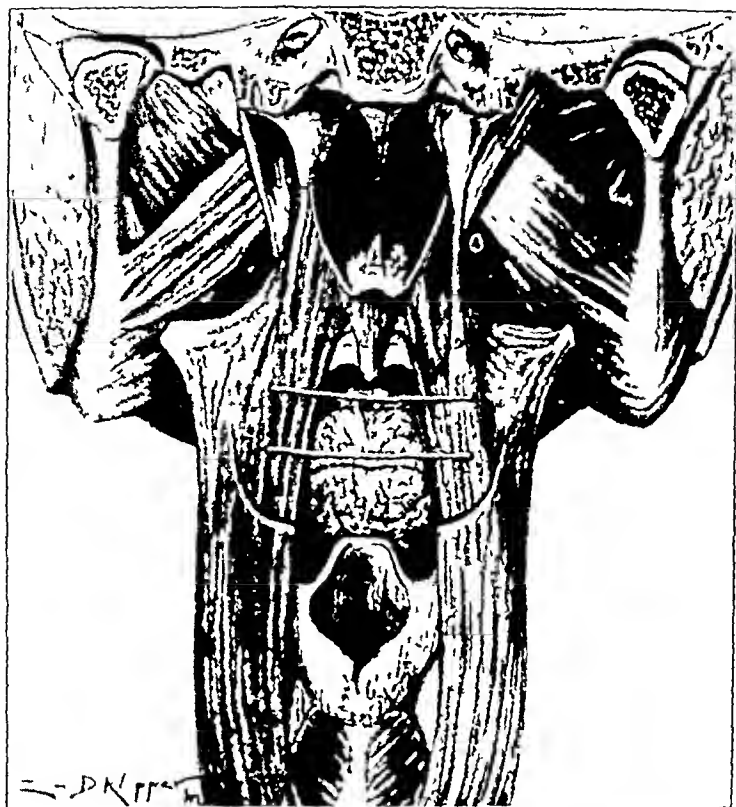


Fig 31—Manner of lengthening palate by utilizing portion of pharyngeal muscles The posterior view is shown with wires in place (From Brophy)

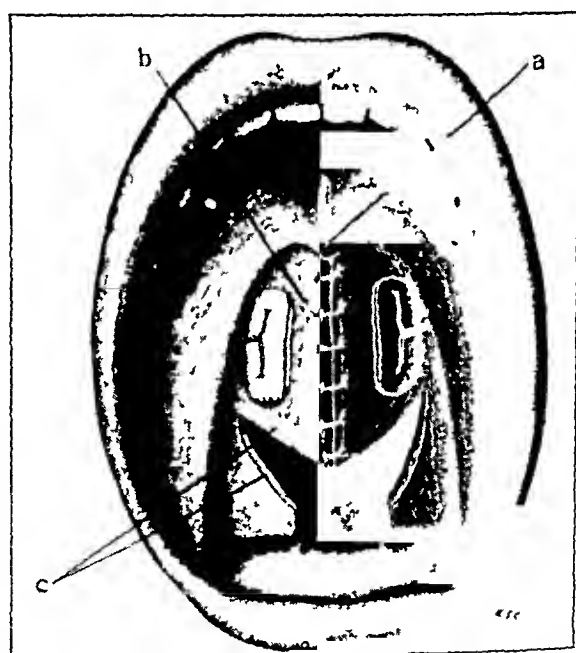


Fig 32—Manner of lengthening the palate by utilizing the palatopharyngeal muscles, after Makuen's method *a* indicates the end of the uvula muscle, *b*, right palatopharyngeal muscle, *c*, incision made through two-thirds the width of the muscle The lead plates are shown with the silver wires twisted so as to approximate the edges of the wound (From Brophy)

formation of a long uvula merely adds a dependent pendulum from the free border of the velum and in some cases may be of more annoyance to the patient than of help

Schoenborn,<sup>77</sup> impressed by the experiments of Tiendelenberg, in 1875 performed velopharyngoplasty to obtain the desired function of the nasopharynx during speech. He outlined a rectangular flap from 4 to 5 cm long by 2 cm wide on the posterior wall of the pharynx. This flap was then elevated with the underlying tissue, turned downward on its pedicle, and trimmed triangularly to fit into the cleft of the velum (fig 34). The velum was freshened and united on either side with the edges of the pharyngeal flap. Schoenborn later decided that the tissue above the superior constrictor muscle of the pharynx was not suitable for his purpose and in 1886 he took the flap with the pedicle directed upward from the tissue of the superior constrictor muscle. This method was recently revived by Rosenthal<sup>78</sup> who in 1924 performed velopharyngoplasty.

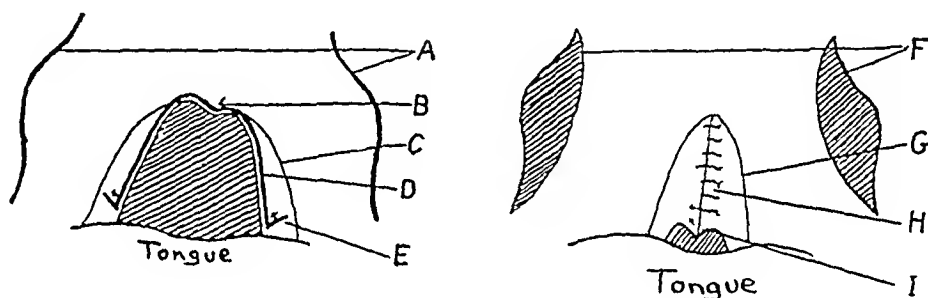


Fig 33—Use of the palatopharyngeal arch for lengthening the velum (After Helbing). A indicates the lateral incisions, B, "rest" of uvula, C, anterior pillar, D, posterior pillars and uvula freshened, E, transverse incision into palatopharyngeus muscle, F, areas to fill with granulations, G, anterior pillars, H, newly formed velum, I, newly formed uvula.

In 1876, Rutenberg<sup>79</sup> proposed that the pharyngeal wall be brought forward so as to enable it to be reached by the velum, thus producing velopharyngeal closure. In order to secure this, he suggested scarifying a semicircular area measuring from 0.5 to 1 cm in width on the mucosa covering the pharyngeal wall, and extending from one hamular process to the other. Rutenberg later added that this method was inadequate in many cases, and suggested that in addition to the scarification as previously outlined, the denuded area might be sutured in a longitudinal direction after the method used in colporrhaphy (fig 35). Scarification may be done either with a knife, the galvanic cauter or chemicals.

77 Schoenborn. *Verhandl d deutsch Gesellsch f Chir* 4 235 1876

78 Rosenthal. *Zentralbl f Chir* 51 1621 1924

79 Rutenberg. *D C Wien med Wchnschr* 26 815 839 and 862 1876

Whenever the tissues forming the pharyngeal wall are utilized to correct palatal insufficiency, scar tissue is always formed, and this will interfere with the forward pull of the superior constrictor muscle of the pharynx. It has been definitely shown that by systematic speech training the uppermost portion of the pterygopharyngeus muscle can be developed into a much more prominent ridge than can be obtained by any operative procedure.

Forbes,<sup>80</sup> of Philadelphia, in 1879, while closing clefts of the uvula, attempted to lengthen the velum by using a curved incision similar to that used by Nélaton for partial cleft lip operations (fig. 36)

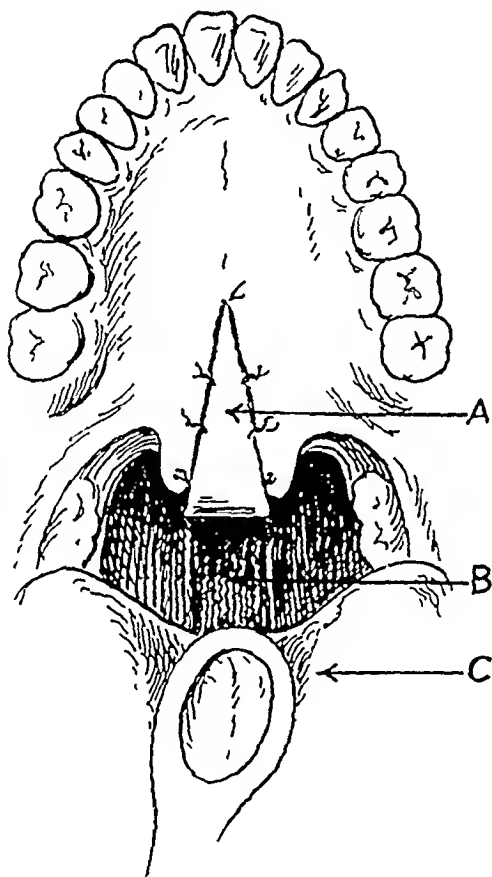


Fig. 34—Artist's conception of Schoenborn's velopharyngoplasty. *A* indicates the pharyngeal flap trimmed triangularly, *B*, denuded area on pharyngeal wall, *C*, dorsum linguae.

Kuster<sup>81</sup> performed an operation in 1882 in which he employed lateral incisions similar to those used by Mirault for cleft lip operations (fig. 37). This procedure, as can be seen from the illustrations, makes a long trilobate uvula. He stated that if this did not produce the desired function sought, the shirt stud-shaped obturator of Passavant might be employed with complete satisfaction.

<sup>80</sup> Forbes, W. S. *Tr. Coll. Phys. Philadelphia* **1** 70, 1875.

<sup>81</sup> Kuster, E. *Berl. klin. Wchnschr.* **19** 172, 1882.

Frankel,<sup>15</sup> in 1882, first suggested advancing the attachment of the superior constrictor muscle of the pharynx by altering the position of its insertion. He did not outline any method to secure this, although he did refer to using the same principle employed in treating strabismus.

Wolff<sup>16</sup> of Berlin, in 1885, advised the use of Schlitsky's soft rubber pharyngeal obturator (fig. 38) after successful cleft palate operations.

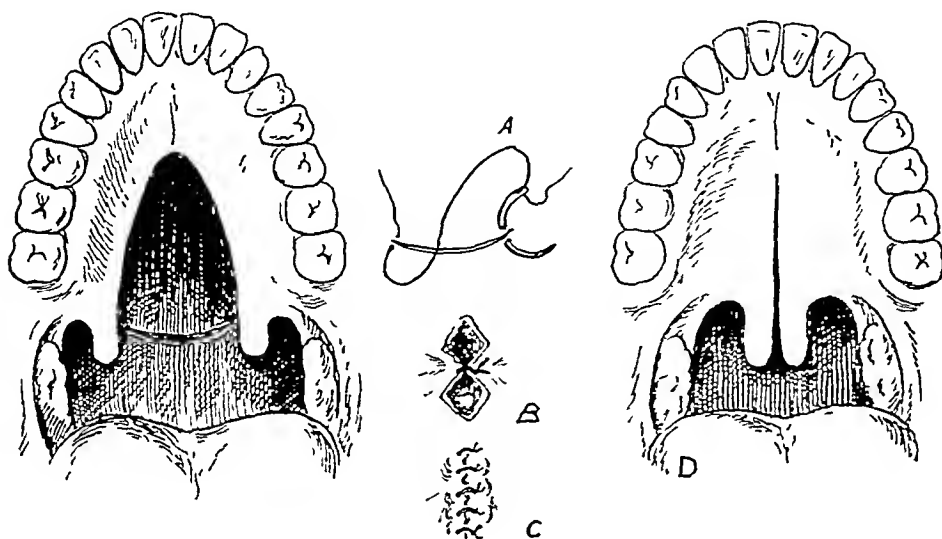


Fig. 35—Artist's conception of Rutenberg's operation to bring the pharyngeal wall forward. *A* indicates the suture through the extremities of incision to produce vertical approximation, *B*, *A*, after knotting of suture. *C*, incision sutured vertically, *D* shows how sides of the cleft approximate after vertical suture of incision as shown in *C*.

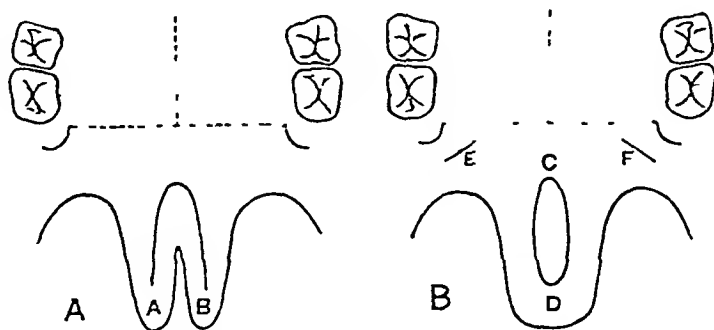


Fig. 36—Forbes' operation. A diagram of the bifid uvula is shown in *A*. The incision is represented by the line *A B*. The bifid uvula after operation is shown in *B*. *C D* indicates the oval wound left to heal by granulation, *E F*, the incisions for division of the palatine muscles. (From Forbes.)

in all cases in which the velum was too short to reach the wall of the pharynx. He discarded this obturator, however, in 1894 for Hahn's hollow hard rubber pharyngeal obturator which except for material was constructed very much as was Schlitsky's obturator.

Billroth,<sup>60</sup> in 1889, was the first to advise dividing the hamular process in cleft palate operations for the purpose of releasing tension on the line of suture. He stated that this permitted the velum to hang freely during its attempts at closure of the nasopharynx.

In 1893, Mears,<sup>9</sup> of Philadelphia, divided the tensor palati, palatopharyngeus and palatoglossus muscles in a case in which the velum was too short to approach the pharyngeal wall. Mears reported that there was marked improvement in the speech of his patient, a young lady who suffered from congenital velopharyngeal insufficiency.

In 1895, Smith,<sup>82</sup> of Nashua, New Hampshire, devised an operation by which uranostaphyloplasty was accomplished with backward dis-

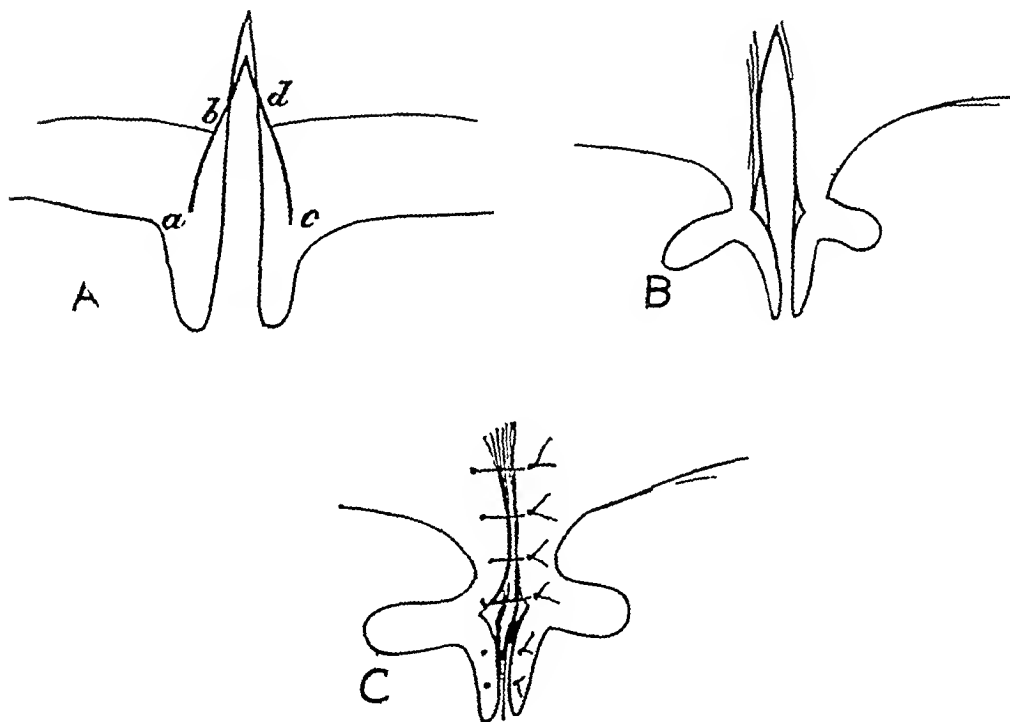


Fig 37—Kuster's operation. In *A*, *ab* and *cd* are cross-incisions running into the full thickness of the velum. In *B*, the velum is displaced backward and made longer. *C* shows *B* after the application of sutures. (From Kuster.)

placement of the velum, permitting it to reach the pharyngeal wall. Smith described his operation in the following words:

From the anterior end of the cleft an incision is made running outwards and a little backwards towards the alveolus, about one-third the distance to the teeth, when the direction of the incision is changed so that it is carried in a straight line nearly to the posterior extremity of the alveolar process (fig 39 *A*). The point at which this incision ends varies with the case, care being taken that sufficient tissue is left for the blood supply of the flap. A corresponding incision having been made upon the opposite side, the two flaps thus outlined are dissected

<sup>82</sup> Smith, Herbert L. Boston M. & S. J. **132**: 478, 1895, Tr. New Hampshire M. Soc. 1905, p. 227, Am. J. Surg. **20**: 65, 1906.

up from the bone, the periosteum being included, and are freed completely from the posterior edge of the palate bones. This last act is very important as only thus can the velum be carried backward and so lengthened. An incision is now made on either side beginning at the point near the last molar where the preceding incision terminated and running along in a curve close to the roots of the teeth as far forward as is necessary or as is deemed safe, sufficient space being left in front for the nourishment of the flaps. This cut usually terminates near the lateral incisors (fig 39 *B*). There are thus formed two triangular flaps composed of mucous membrane and periosteum which are carried into the median line and

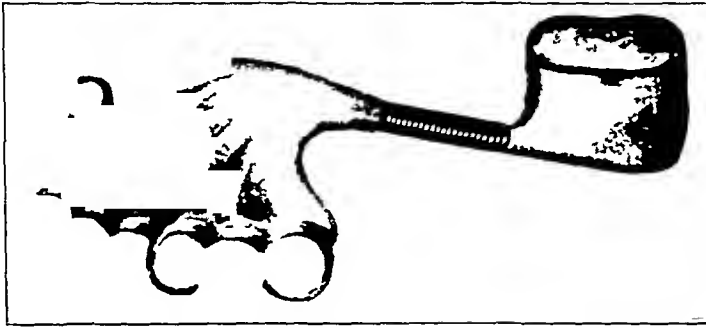


Fig 38—Schlitsky's obturator (After Partsch)

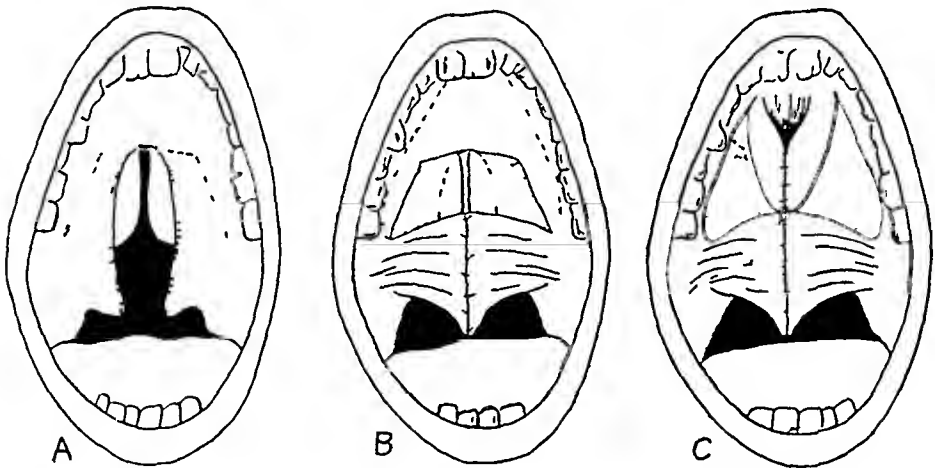


Fig 39—Smith's operation for lengthening the velum (From Smith)

sutured together. The freshened edges of the velum are now sutured and the posterior edges of the anterior flaps are sewn to the middle of the newly formed velum (fig 39 *C*). If deemed best, tension can still further be guarded against by extra sutures placed in the velum at the same distance from the edge. In case there seems danger that the palate may be carried too far forward during the process of repair through contraction of the flaps, it has seemed to the writer quite feasible to pass a suture through the periosteum at the posterior edge of the palate bones, and thus anchor the velum at the desired point.

Gutzmann<sup>25</sup> of Berlin, in 1899 advised massage of the velum with an apparatus which conformed with the contour of the palate (fig 40)

The loop of this instrument was covered with gutta-percha. Gutzmann also advised that systematic speech training should be instituted as an adjunct to any form of treatment for cleft palate.

Geisuny, in 1900, suggested the possibility of advancing the posterior wall of the pharynx to secure velopharyngeal closure by injecting soft paraffin into the retropharyngeal space (fig 41). This method was modified in 1902 by Eckstein,<sup>83</sup> who substituted hard paraffin. The ill effects arising from the use of paraffin in the retropharyngeal space were later pointed out by Lexer, Wainekios, Rose and von Gaza.

Philip,<sup>30</sup> in 1904, reported favorable results by the use of the faradic current on the posterior pillars. He advised that the electricity be used in conjunction with speech exercises and suggested this treatment in all cases of congenital insufficiency of the palate.

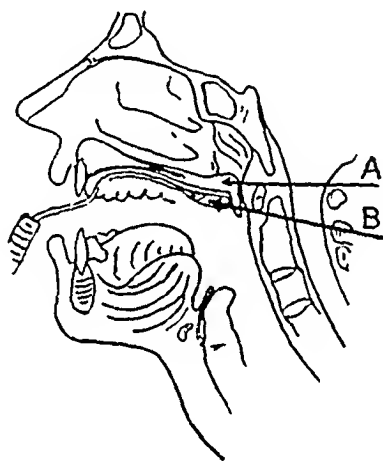


Fig 40—Gutzmann's hand obturator (After Nadoleczny). *A* indicates the velum against the posterior wall of the pharynx, *B*, the hand obturator in position.

In 1907, Boley<sup>10</sup> suggested narrowing of the velopharyngeal space by reducing the length of the curve inscribed by the pharyngeal wall at the level where contact of the velum with the wall of the pharynx is desired. To accomplish this, he outlined with silver nitrate on the median part of the pharyngeal wall, an ellipse running with its long axis in the vertical plane (fig 42 *A*). This ellipse measured from 30 to 40 mm in its longitudinal diameter and from 15 to 16 mm in its transverse diameter. The elliptical area was then excised and the edges of the wound united by suture (fig 42 *B*).

In 1911, Blain,<sup>35</sup> of St. Louis, developed an autoplasmic method in which he made use of the side incisions employed by Kuster to overcome further shortening of the velum in cases in which the soft palate

<sup>83</sup> Eckstein. *Berl klin Wchnschr* 39 315, 1902.

was too far forward from the pharyngeal wall. Blain described his operation in the following words:

Kuster proposed the plan by means of the incisions *b-b* (fig 43*A*) of lengthening the velum, but there is rarely sufficient palate tissue to permit this being done without leaving such wide gaps at the site of the lateral incision that subsequent scar contraction renders the velum too tense to move freely. The figure 43*A* shows a modification which obviates the latter difficulty.

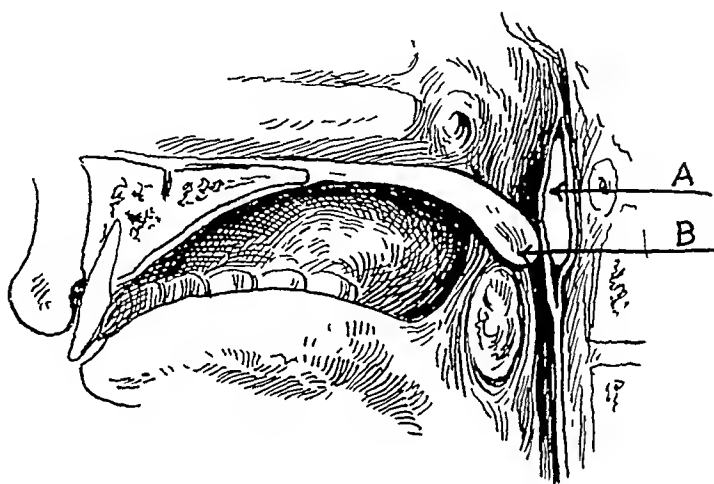


Fig 41—Artist's conception to show how the injection of paraffin by Gersuny and Eckstein may produce bulging of the posterior pharyngeal wall. *A* indicates the paraffin in the retropharyngeal space, *B*, the velum.

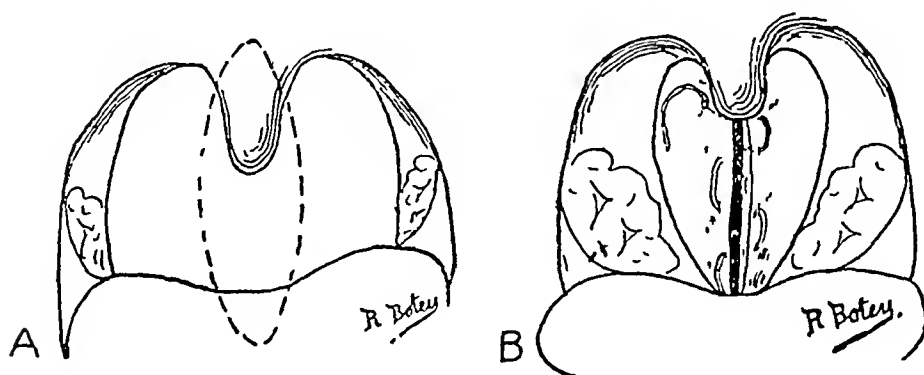


Fig 42—Narrowing of the pharyngeal canal (After Botey). In *A* Botey shows the elliptical incision made use of in his operation, in *B*, suture of the wound in the posterior wall of the pharynx by the continuous suture.

*A* (fig 43*A*) shows incision at the lateral border of the hard palate through the mucoperiosteum carried beyond the maxillary tubercle and straight out on the buccal mucosa for 1.5 cm, then backward to the level of the lower jaw and then inward, again cutting the pterygomaxillary ligament. The mucosa pterygomaxillary ligament and the buccinator muscle are cut through and the flap is dissected up until the space between the internal pterygoid and tensor palati muscle is opened. The hamular process is cut through at its base.



The cleft borders of the velum are not freshened in the usual way but the incisions *b-b* (fig 43A) are made on either side through the whole thickness of the soft palate and the flaps behind these incisions are rotated backwards. In this way the incisions *b-b* are opened and the raw surfaces thus exposed are sutured to each other at the median line (see *b*, fig 43B). As the two halves of the velum are carried toward the median line, the flaps *a-a* are drawn inward and there will be no subsequent scar contraction to render the velum tense and comparatively useless. The space between the upper and lower jaw is still cov

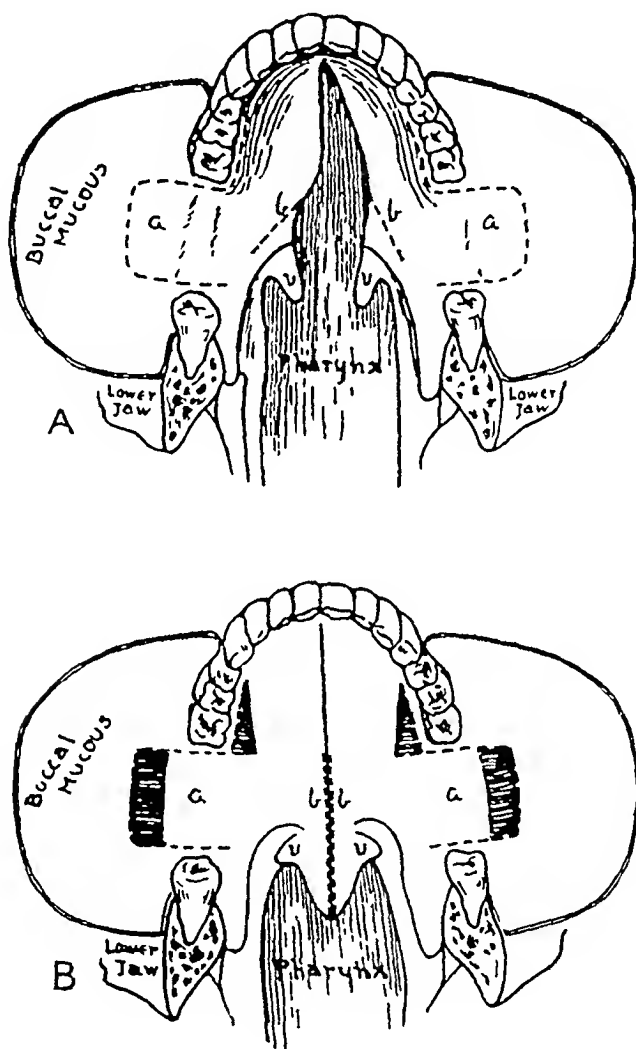


Fig 43—Blair's operation (From Blair)

ered and opening of the mouth is but slightly interfered with. This operation gives a longer velum than is obtained by the simple Langenbeck operation and therefore a better functional result is obtained. It will not permanently cripple the action of the superior constrictor muscle of the pharynx.

Pickerill,<sup>84</sup> in 1912, developed a procedure by which surgical measures were combined with prosthesis to correct anteroposterior shortening of the palate when the shortening was the result of scar

84 Pickerill, H. P. New Zealand M. J. 11: 125, 1912.

contraction following a cleft palate operation. The method consisted in altering the cleft velum into a muscular bridge running across the roof of the mouth. This was accomplished by freshening the velum on one side of the cleft and applying a side incision into the velum running anteriorly through its posterior border as shown by *A* and *B* in the figure 44 *A*. The other side of the cleft was prepared by freshening its posterior border *C* and a similar lateral incision was made, as represented by *D*. These flaps were swung across the roof of the mouth and united with suture so as to obtain the muscular bridge as shown in figure 44 *B*. The sutures were removed on the tenth day. Two

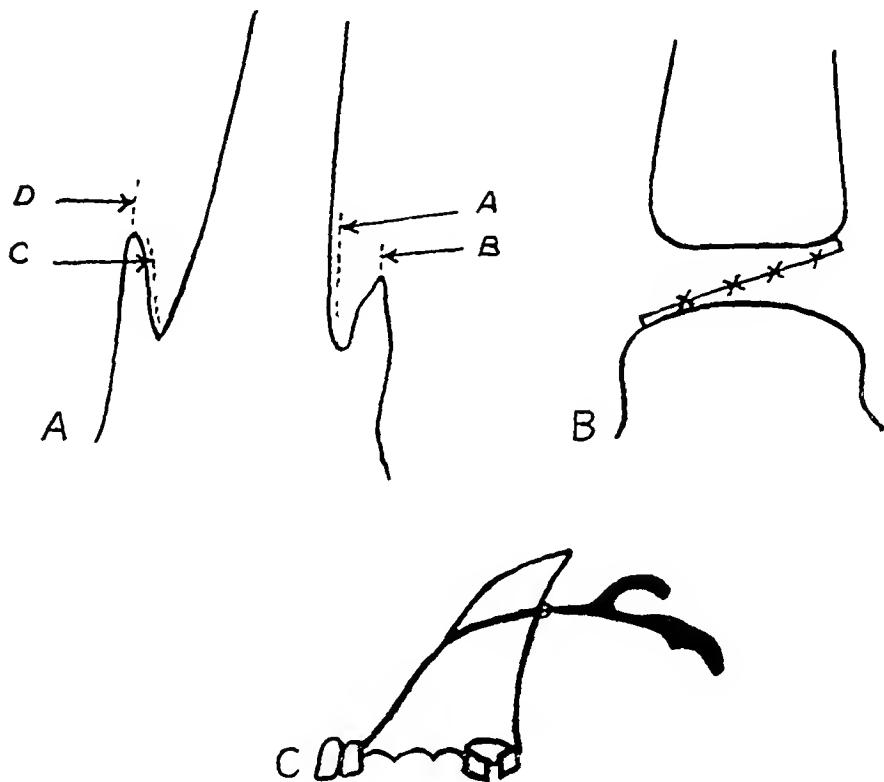


Fig 44—Pickerill's method of combining palatoplasty with prosthesis. *A*, dotted lines, the margins to be pared and the lateral incisions. *B*, flaps running across and sutured in position. *C*, diagram of appliance used to fill up the cleft, showing the hook by which the hinged velum is attached to the muscular bar and also an artificial vomer attachment.

weeks later the obturator-velum shown in figure 44 *C* was constructed. The velum of this appliance was made of hard vulcanite with a hook placed on its nasal aspect. The velum was attached by a platinum hinge to an obturator plate fashioned to cover the defect in the hard palate and attached to the teeth. The obturator plate could be fitted with an artificial septum in cases in which the septum naris was absent. The principle of this appliance was such that the hook rested

on the muscular bridge which raised the velum and depressed it as the muscles were brought into play. The velum was also embraced by the superior constrictor muscle of the pharynx during phonation and deglutition.

Naegeli,<sup>85</sup> in discussing Pickerill's method in 1924, stated that three patients were treated in Gailé's clinic with marked success.

In my opinion, this operation is impracticable. From my experience in treating patients with cleft palate, it is better to select either a purely surgical procedure or else fit the patient with an obturator-velum. Either one of these methods, when properly applied, will produce good speech. Pickerill's method destroys and deforms, by scar formation, a velum which would have been useful in treating the cleft by ordinary operative procedures. The use of the obturator-vela is difficult in children on account of their growth and dentition. If, for any reason a child leaves

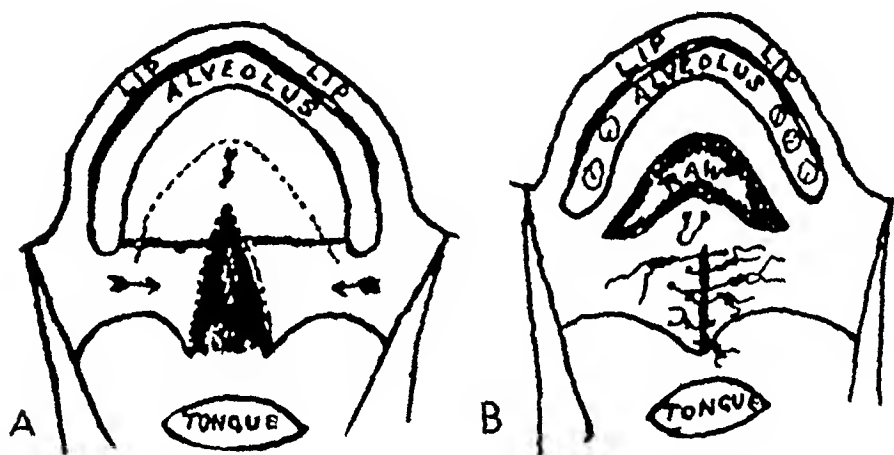


Fig 45—Roberts' operation for lengthening the velum. *A* indicates the "apron" flap for lengthening short velum or closing clefts, using intranasal suture, *B*, "apron" flap and intranasal suture. (From Roberts.)

his appliance out of his mouth for several days, it may be impossible for him to reintroduce it as the teeth frequently undergo such a marked change in their position.

Roberts,<sup>86</sup> of Philadelphia, in 1918 published the report of an operation by means of which he produced backward displacement of the palatine mucoperiosteum which remained in continuity with the velum to secure velopharyngeal closure, in cases in which the palate appeared to be lacking in material or was shortened or stiffened. Roberts made a curved incision across the palatine vault in the region of the canine teeth (fig 45 *A*) and elevated the mucoperiosteum from the underlying bone, freeing the velum from its attachment to the palate bones. This procedure furnished a mucoperiosteal apron suspended from the

<sup>85</sup> Naegeli, T. *Schweiz. med. Wchnschr.* 5:62, 1924.

hamular processes (fig 45 B). The velum was then displaced backward like a sling and held by a looped suture passed through the united palate, the ends of which were passed out through the nostrils, where they were held around a rubber tube at the columella (fig 46).

Veau and Ruppe<sup>86</sup> of Paris in 1922 called attention to the fact that the classic "Bazcan-Langenbeck-Lielat" procedure for performing cleft palate operations left a denuded area on the nasal surface of the palate which on healing produced extensive scar tissue, which on retraction prevented the velum from approximating the posterior pharyngeal wall. These surgeons insisted that separate suturing of the nasal mucoperiosteum, the muscular layer of tissue forming the velum by silver wire suture, and the oral mucoperiosteum prevented this undesirable scar contraction. In order to accomplish this the nasal



Fig 46—Nasal suture holding palate flap in position against bone, shown threaded and tied to rubber tubing at nares. (From Roberts.)

and oral mucoperiosteum must be thoroughly separated from the bony palate. They also advised the use of the V-shaped incision introduced by Ganzer<sup>87</sup> in order to obtain the retiotransposition of the palate.

Rosenthal,<sup>78</sup> in 1924, revived Schoenborn's velopharyngoplasty, which he combined with a modified Langenbeck uranoplasty, for all cases requiring closure of the cleft which involves the hard and soft palate. This combined operation was done at one sitting so as to correct the speech deficiency which so commonly followed ordinary cleft palate operation. In performing Langenbeck's uranoplasty, Rosenthal makes lateral incisions as close to the alveolar border as possible. The incision

<sup>86</sup> Veau, Victor, and Ruppe, Charles. *Rev de chir* 60 81, 1922, *J de chir* 20 1, 1922, *J de med et chir prat* 95 685, 1924.

<sup>87</sup> Ganzer, Hugo. *Berl klin Wchnschr* 57 619, 1920.

extends well behind the last molar tooth, where its direction now follows the pterygomandibular ligament, over which it extends to a point 1 cm from the last mandibular molar tooth (figs 47 and 48) This method of extending the lateral incision was first used by Blair<sup>85</sup> of St Louis in 1911

In February, 1925, Ernst<sup>88</sup> criticized Rosenthal's method, and he suggested circular narrowing of the pharynx so as to permit the velum to approximate the pharyngeal wall Ernst's article contained no illustrations, and it was impossible to make an adequate mental picture of his operation Halle,<sup>89</sup> in May, 1925, gave further details of this operation, which is now known as the Ernst-Halle method The operation is a modified Langenbeck procedure, in which the following steps are added After freshening the edges of the defect the nasal mucosa is separated from the oral mucosa, the lateral incisions are extended well behind the last maxillary molar tooth, then directed backward and downward so that the incisions terminate in the palatopharyngeus arch, mesial to the last molar teeth (fig 49 *A*) An elevator is then introduced in such a manner that it remains in intimate contact with the underlying bone, thus avoiding any injury to the palatal muscles It proceeds behind the superior constrictor muscle of the pharynx, as shown in figure 49 *B* The space thus formed by the separation behind the pharyngeal wall is then packed with iodoform gauze so as to bring about mesial displacement of the lateral walls of the pharynx (fig 49 *C*) These gauze packs are changed from time to time until the cavity is well filled with granulation tissue While waiting for the granulation tissue to form the anterior attachment of the palatine mucoperiosteum is gradually separated behind the incisor teeth by small incisions As soon as sufficient collateral circulation is established, the anterior attachment of the palatine mucoperiosteum is completely divided, as shown in figures 49 *B* and *C* This permits the entire soft tissue of the palate to become displaced backward The anterior portion of the displaced palate is then sutured at the incisor teeth so as to prevent too much backward displacement This procedure secures from 1.5 to 2 cm narrowing of the pharynx, as reported by Halle in cases of incomplete cleft palate When dealing with cases of complete cleft palate, the V-shaped incision of Ganzer<sup>87</sup> is used, as shown in figures 49 *D*, *E* and *F* It appears to me that the Ernst-Halle operation cannot be used in children without accepting a high mortality The V-shaped incision of Ganzer<sup>87</sup> would appear to be ideal, theoretically Practically, however, when one remembers that the palatine mucoperiosteum is not flexible, one readily

88 Ernst, Franz *Zentralbl f Chir* 52 464, 1925

89 Halle *Verhandl d Gesellsch deutsch Hals-, Nasen- u Ohrenh*, May 28, 29 and 30, 1925, *Ztschr f Hals-, Nasen- u Ohrenh* 12 277 1925

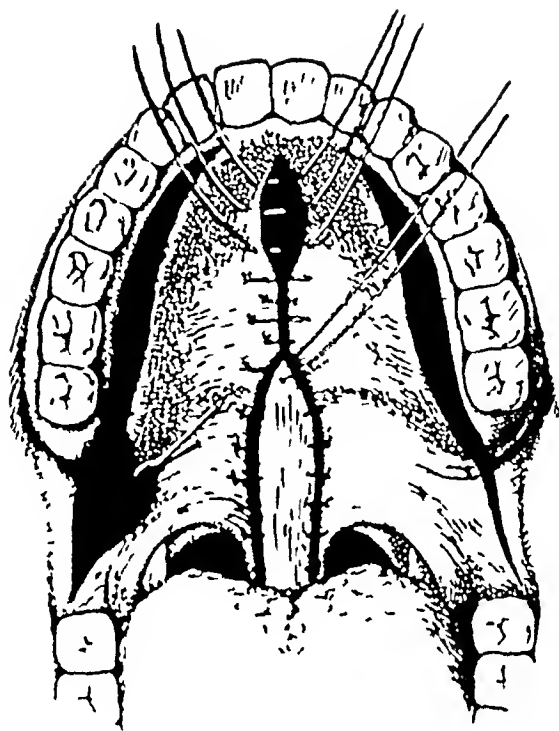


Fig. 47—Oral view of pharyngeal flap and lateral incisions (After Rosenthal)

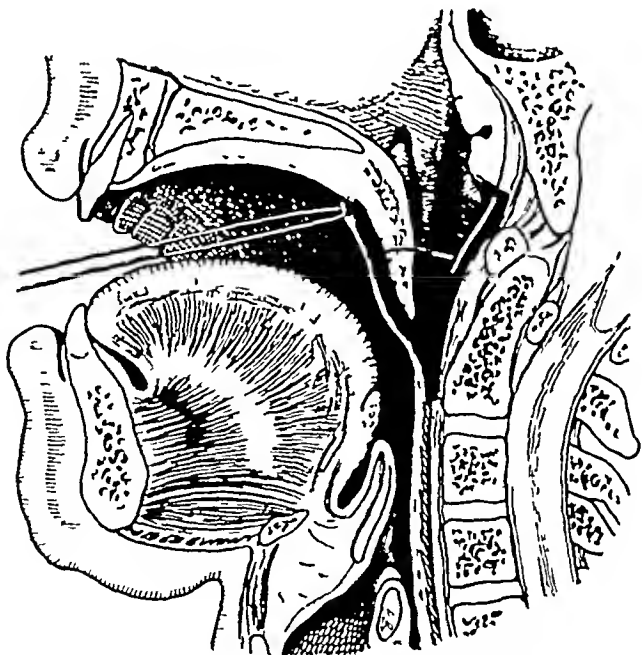


Fig. 48—Sagittal section to show the pharyngeal flap turned downward to fit into the cleft in the velum (After Rosenthal)

realizes that when it is sutured under tension it is bound to tear apart and resume its original position. It has been my experience in plastic surgery that stiff tissue like that of the palatine mucoperiosteum cannot be stretched evenly. By following Ganzer's method in palatine operations, unquestionably puckering of the mucoperiosteum must result.

Von Gaza,<sup>90</sup> in 1926, advised the implantation of fat and fascia tissue into the retropharyngeal space in order to produce bulging of the

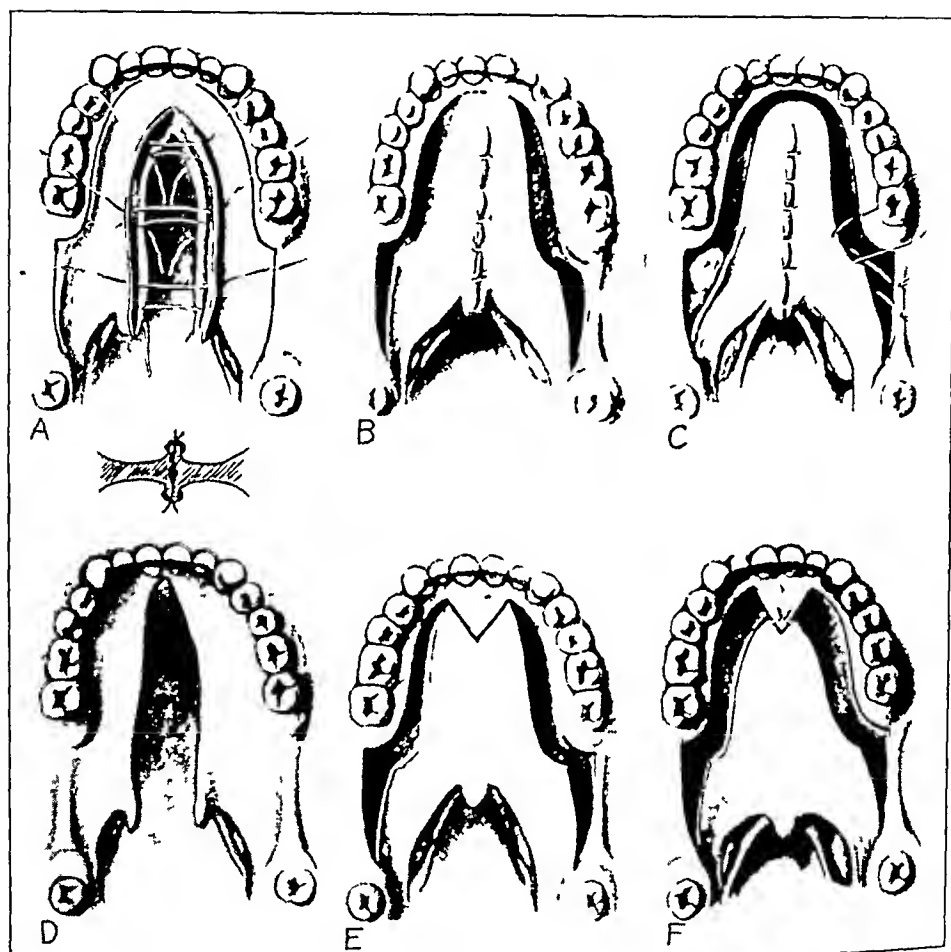


Fig 49—In *A*, the upper figure shows the edges of the defect slit open to separate nasal from oral mucosa, the lower figure shows the sides of the defect approximated with the oral and nasal mucosa sutured separately. *B* shows the defect sutured. The dotted line indicates the incision used to separate the anterior attachment of palatine mucoperiosteum. In *C*, retropharyngeal packing is seen on the right side and the retaining sutures on the left side. *D* shows the cleft palate extending as far anteriorly as the alveolar margin. In *E*, the palate is completely closed in the midline. The V-shaped incision of Ganzer is shown. *F* shows how Ganzer's V-shaped incision is held anteriorly to the mucoperiosteum behind the incisor teeth. (After Halle.)

pharyngeal wall. He condemned the intra-oral method of approach because of fear of infection, and suggested entrance through the neck.

<sup>90</sup> Von Gaza, W. Arch f klin Chr 142 590, 1926

by way of the superior lateral triangle. He obtained the fat and fascia from the abdomen or gluteal region except in children for whom he advised the use of the fascia lata. The operation consists of making a curved incision from 3 to 5 cm. in length dividing the skin, superficial fascia and platysma muscle the incision being made one fingerbreadth from the mastoid process just below the lobe of the ear and in front of the anterior border of the sternocleidomastoid muscle (fig. 50). The incision extends as far down as the angle of the mandible. The tissue behind the jugular vein is removed by blunt dissection. Entrance into the retropharyngeal space (figs. 51, 52 and 53) is made by proceeding inward, forward and upward using as a guide the tendons of the longus capitis and longus colli muscles which lie anterior to the vertebral column at the level of the third cervical vertebra. The pharyngeal wall is pushed forward by the finger and separated from the prevertebral tissues on both sides. The cavity formed by this separation is then

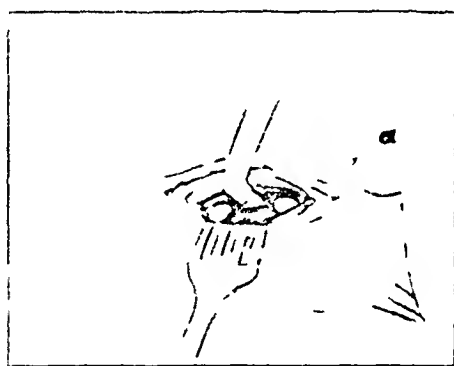


Fig. 50—Incision exposing the cervical glands with the vascular and nerve bundles drawn aside. The longus colli muscle is exposed. (After von Gaza.)

temporarily packed with gauze to control bleeding. Later, the gauze is replaced by the transplant. Von Gaza mentioned the fact that Perthes suggested the use of cartilage transplants into the retropharyngeal space for the correction of velopharyngeal insufficiency. The operation in the hands of von Gaza appears to be a simple, bloodless procedure. In my opinion, however, it calls for a great deal of skill and is not without danger. When the operation is performed on children, it has one point in its favor in that it will free the superior constrictor muscle of the pharynx, thus permitting it to come forward. Nevertheless when a graft is introduced into the retropharyngeal space in a child the implanted tissue will not grow in size; in fact, it will tend to shrink, whereas the pharyngeal canal will increase in size. I feel that the method is not justified in the average case, as Passavant's cushion can be increased in size by such simple procedures as massage, electricity and speech training.



Kirkham,<sup>91</sup> in 1927, pointed out that in cases of cleft palate the distance between the hamular processes is greater than in normal mouths. He further stated that the increase is in proportion to the width of the cleft. In his opinion, velopharyngeal insufficiency is due more to the widened condition of the pharynx than to the shortened state of the velum. Kirkham reached his conclusion after making mea-

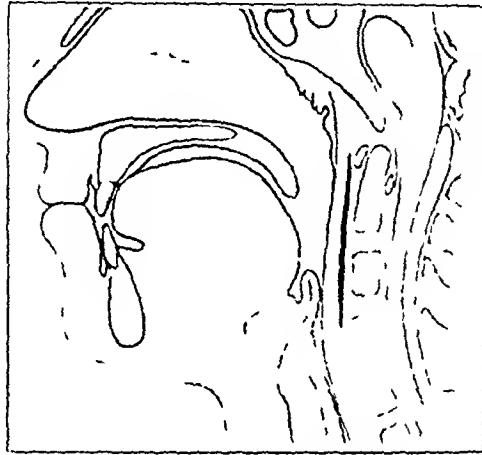


Fig 51—Sagittal section, showing retropharyngeal space to receive fat tissue (After von Gaza)

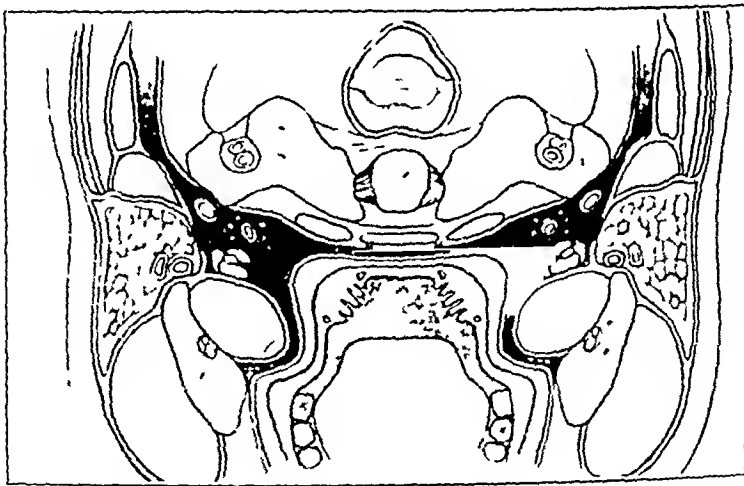


Fig 52—Horizontal section at the level of the second cervical vertebra, showing loose tissue behind the pharyngeal wall. The dark area shows areolar tissue (After von Gaza, modified from Corning)

surements of normal specimens of the palate and comparing these with specimens of cleft palate of the same age at the Hunterian Museum of the Royal College of London. Basing his operation on these observations, Kirkham shortened the superior constrictor muscle of the pharynx.

<sup>91</sup> Kirkham, H. L. D. *Surg. Gynec. Obst.* 44: 244, 1927.

so as to permit it to contract more forcibly. The operation consisted of freshening on either side the upper edge of the superior constrictor muscle and suturing this to the corresponding freshened side of the palatopharyngeus muscle (fig 54). This operation was performed by Kirkham in a boy 6 years of age and was a complete failure.

Woods<sup>92</sup> in 1927 published an article in which he reported success with the injection of paraffin into the retropharyngeal space in cases in which the velopharyngeal opening remained moderately small after a standard cleft palate operation. He also used a method analogous to that of Rutenberg which he describes in the following words:

In 1925 I was consulted by a lady, age 30 years, on whom quite a good operation had been performed but the opening behind the palate was literally huge. She felt her disability quite acutely and was most anxious that something should

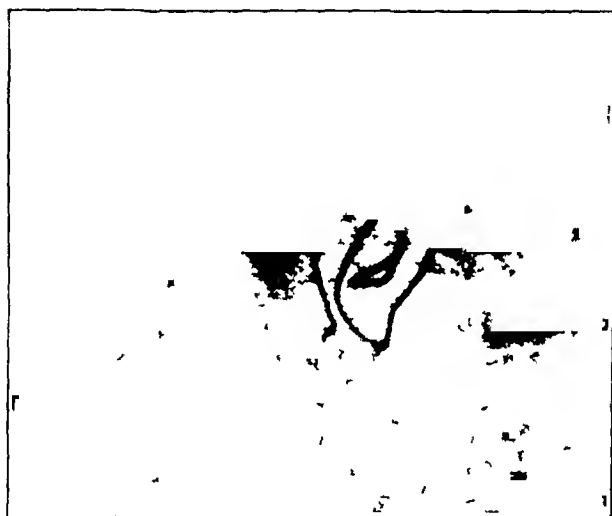


Fig 53—Roentgenogram showing a gold thread placed in the transplanted fat tissue. The pharyngeal wall has been brought forward. (After von Gaza.)

be done. I consented to try. I thought by snipping away the mucous membrane of the nasopharynx at the level of the palate, so as to form a linear wound there might be some hope that, after cicatrization when the scar contracted, the defect might be so reduced that she could completely cure it by training the muscles. I accordingly snipped away a ring of tissue but the result was most disappointing as the remedy proved quite futile. The wound healed with the most aggravating rapidity, leaving her neither better nor worse for the attempt.

This failure was followed by the use of diathermy. From the latter procedure, Woods claimed a fair amount of success. From Wood's description of the application of diathermy, one is led to believe that he meant electrocoagulation. He describes the treatment in these words:

I next tried diathermy. This produced a slough of the superficial tissues of the sides and back of the pharynx and the edge of the soft palate, including the

uvula The throat was very sore and painful for some days She had no rise in temperature After a week or so the wound cleared up and contraction began This continued until about three months later The wound was reduced to the size of the tip of the small finger I found then that it was quite easy for her to close it completely by an effort of the will She thus had all the physical conditions necessary for normal speech

Limberg<sup>13</sup> of Leningrad, in 1927, criticized the Einst-Halle procedure for obtaining reposition of the palate, this criticism being directed at the fact that they divided the posterior palatine vessels and

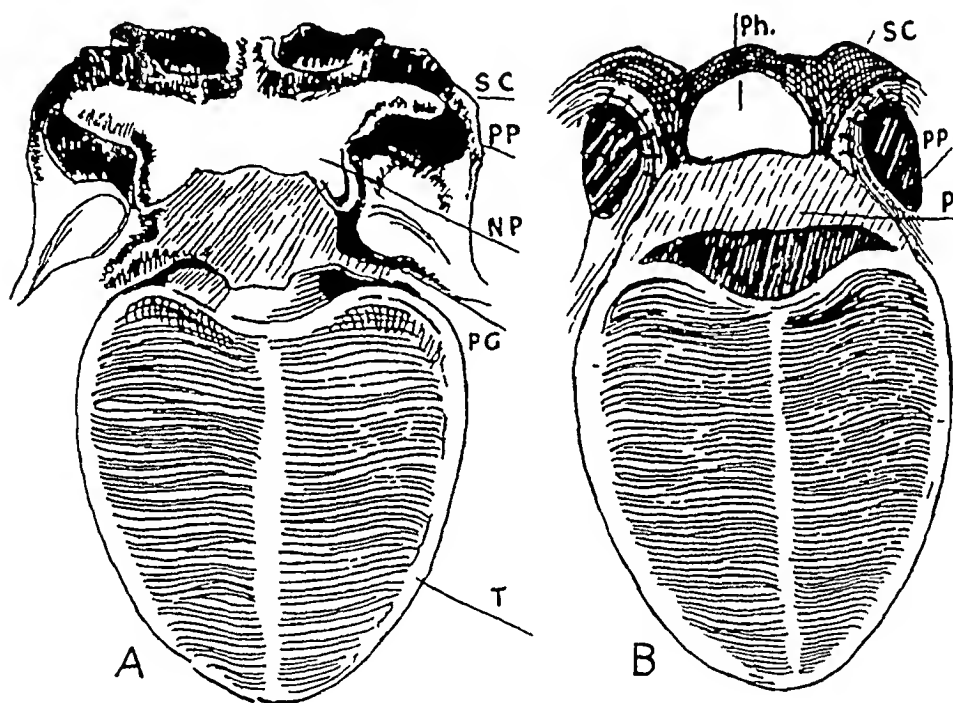


Fig 54—*A* is a cross-section of the nasopharynx just above the level of the uvula *SC* indicates the superior constrictor, *PP*, palatopharyngeus, *NP*, nasopharynx, *PG*, palatoglossus, *T*, tongue *B* shows diagrammatically a cross-section of the point where the superior constrictor was sutured to the posterior surface of the palate and the palatopharyngeus muscles *Ph* indicates the pharynx, *SC*, superior constrictor, *PP*, palatopharyngeus, *P*, palate (From Kirkham)

nerves To preserve the continuity of these structures and to secure complete relaxation of the soft tissues of the palate with its backward displacement, Limberg proposed two formidable operations The first of these methods consisted of resection of the greater palatine foramen and interlamina osteotomy of the pterygoid process The second procedure was accomplished by pterygomaxillary osteotomy

Resection of the greater palatine foramen was accomplished by means of the chisel or bone-cutting forceps, cutting mesially and posteriorly to the foramen so as to release the vessels and nerves and displace them inwardly and posteriorly (fig 55)

Interlamina osteotomy of the internal pterygoid plate is performed by placing the chisel on the palate bone external to the greater and lesser palatine foramina. The cutting edge is directed parallel with the perpendicular plate of the palate bone in such a manner as to resect the internal pterygoid plate from the external at their point of articulation with the palate bone. This resection permits mesial transposition

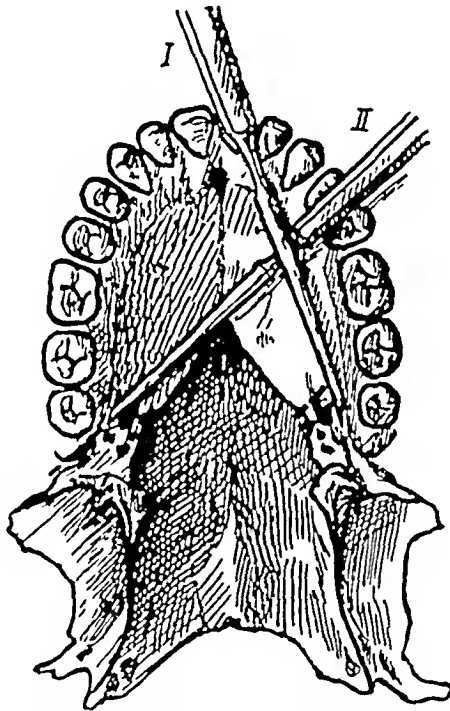


Fig 55—I shows how interlamina osteotomy is made, II, how pterygo-maxillary osteotomy is made (From Limberg)

of the mesial pterygoid plate with its hamular process, and keeps the anatomic continuity of the vessels and nerves intact (fig 55). Pterygo-maxillary osteotomy was accomplished by introducing the chisel through the horizontal plate of the maxilla between this bone and the pterygoid plate. The process was then separated and moved inward toward the mesial line. While Limberg preserves the relation of the posterior palatine vessels and nerves, as has been already pointed out, all surgeons agree that it is impossible to liberate the palatine mucoperiosteum and secure the desired backward displacement without injury to these vessels and nerves. From my experience in the operating room, and from postmortem studies of operative cases, as well as anatomic studies,

I am convinced that the nerves and vessels are usually divided during cleft palate operations. I further believe that no injury results to the patients from the division of these structures.

In May, 1928, Moorehead,<sup>93</sup> of Chicago, published an article in which he described an operation for correcting secondary palatine defects by using lateral incisions similar in principle to those used by Ernst-Halle and by myself<sup>94</sup> for gaining repositioning of the velum to correct cleft palate speech. The V-shaped incision described by Moorehead was first suggested by Ganzer<sup>87</sup> before 1920 and later modified by Ernst and Halle in 1925 (fig. 56).

In 1928 Wardill<sup>95</sup> developed a two-stage operation by which he combined narrowing of the pharyngeal canal with closure of the existing cleft in the palate to establish a good speaking voice. The first stage

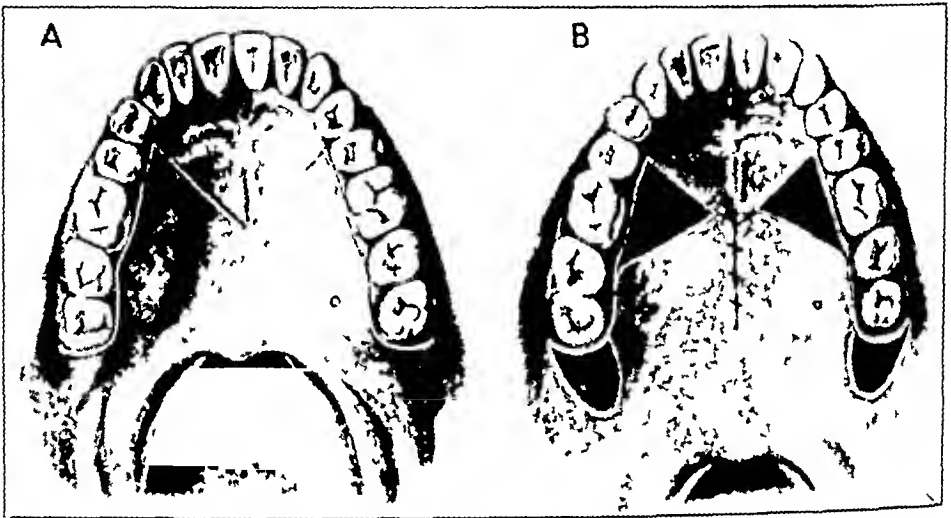


Fig. 56—Method of transposing the palate to (A) lengthen the palate and (B) release tension and make possible the closure of the nasopharynx in speech (After Moorehead)

of this operation is analogous to that of Rutenberg and consists in narrowing the nasopharynx laterally with the production of a more prominent Passavant cushion. Wardill described this step of the operation in the following words:

The patient, lightly anesthetized, is laid upon the back with a pillow beneath the shoulders and the head thrown well backwards. The mouth is held open with a gag. The pharynx is stimulated and the position of the ridge of Passavant is noted. With a fine tenotome, the mucous membrane is incised trans-

93 Moorehead, F. B. Correction of Secondary Palate Defects. *J. A. M. A.* **90**: 1614 (May 19) 1928.

94 Dorrance, George M. *Ann. Surg.* **82**: 208, 1925, *I. Am. Dent. A.* **14**: 1112, 1927.

95 Wardill, W. E. M. *Brit. J. Surg.* **16**: 127 (July) 1928.

versely at the level of the ridge of Passavant, i. e., over the anterior arch of the atlas, and is then held open with fine sharp hooks (fig 57*A*). Care is taken not to incise too deeply and thus open the loose areolar tissue between the buccopharyngeal and prevertebral layers of fascia. The buccopharyngeal fascia is relatively tough, and the superior constrictor muscle and its covering mucosa can be readily peeled or scraped from it by means of blunt dissection with a curved aneurysm needle. The dissection is carried on in this layer, upwards nearly as far as the base of the skull, downwards for a similar distance, and laterally beyond the ridge caused by the salpingopharyngeus muscle. During the whole of this part of the operation some resistance is felt to the dissection. If this resistance is not felt, it is probable that the point of the needle is in the loose retropharyngeal cellular tissue.

Using the aneurysm needle as a combined director and retractor, the incision is enlarged laterally right up to the salpingopharyngeus by the use of a curved

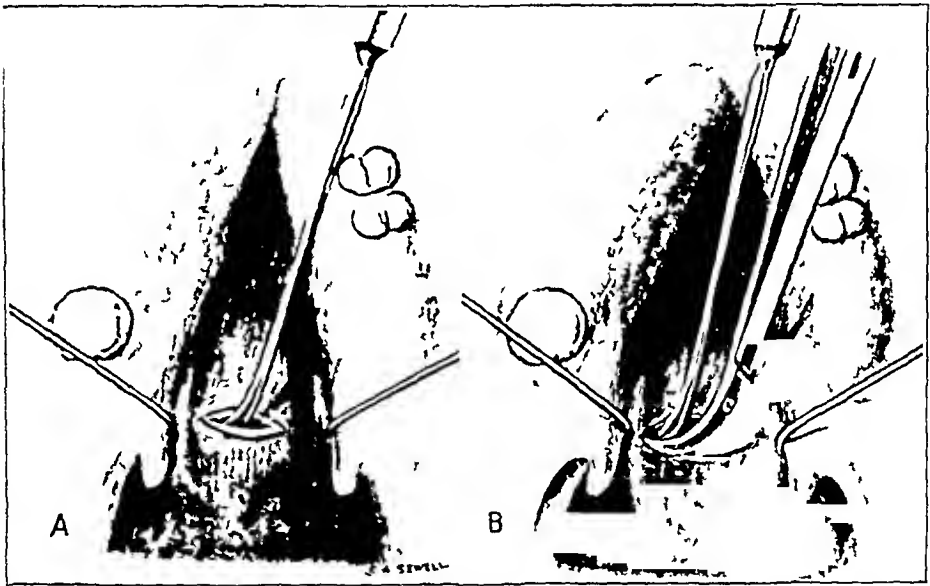


Fig 57—*A* shows separation of the superior constrictor from the buccopharyngeal fascia, *B*, extension of the incision as far as the salpingopharyngeus. (From Wardill.)

scissors (fig 57*B*). Bleeding is very small in amount, there being no more than a slight ooze. The business of sewing up the incision in a vertical direction is now undertaken. I have had a small spring wire retractor made (fig 58) for the purpose of facilitating this procedure. The retractor holds the incision open in a vertical direction. Using very small curved needles made on the Mayo principle, sutures of No 0 catgut are inserted, commencing first at the upper and lower ends of the wounds, the sutures are left long and may be used as retractors. It is important to take big bites of tissue on each side, as the sutures have a tendency to work out very quickly. The suturing is completed in the center of the wound by joining together the salpingopharyngeal folds, including a sufficient bite to obtain a firm hold of the tough connective tissue which is intimately bound up with these (fig 59). Usually a suture is passed through the posterior pillars of the fauces for the purpose of relieving the tension for a few days. At

the end of the operation the halves of the soft palate are found to be much closer together, and the halves of the uvula may overlap. In fact, one wonders how the patients are going to be able to swallow.

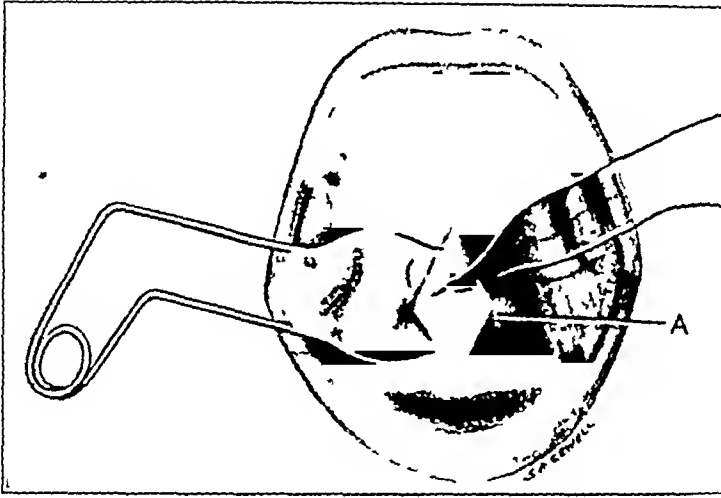


Fig 58—Suture of the wound in a vertical direction. *A* shows the edge of the salpingopharyngeal fold. (From Wardill)

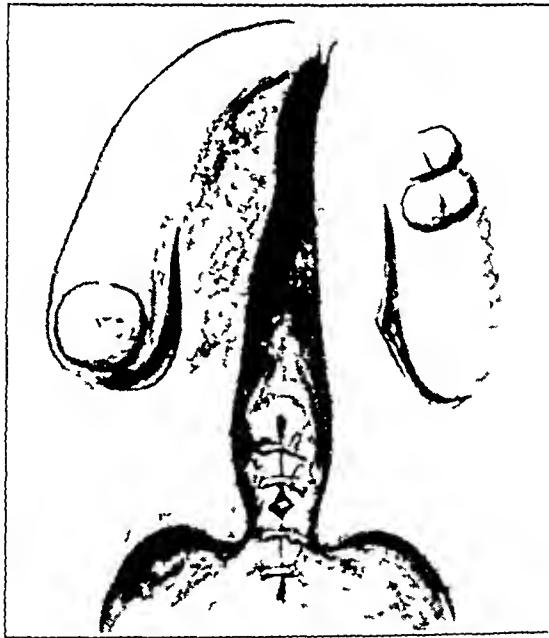


Fig 59—First stage of the operation completed. Lateral incisions were made for Langenbeck-Fergusson repair. (From Wardill)

#### CONCLUSION

Several years ago, I was confronted with a case of congenital short palate, a condition for which no known treatment had succeeded in obtaining normal speech. I visited many of the well known clinics

of Europe and the United States. The consensus among cleft palate operators appeared to be that where a long velum was present excellent results could be obtained with any standard cleft palate operation, i. e., the Langenbech operation or any of its modifications.

All agreed that failures in cases occurred in which velopharyngeal closure was insufficient. The failures in these cases consisted chiefly in speech defects. The patients could not speak any better after the operation than before. The inability to correct the speech deficiency in congenital insufficiency of the palate was the reason for this study.

A complete survey was next made of all methods employed for correcting this defect. I was dissatisfied with all the methods that had been suggested. No operation appeared applicable in every case, and many of these operations were useless.

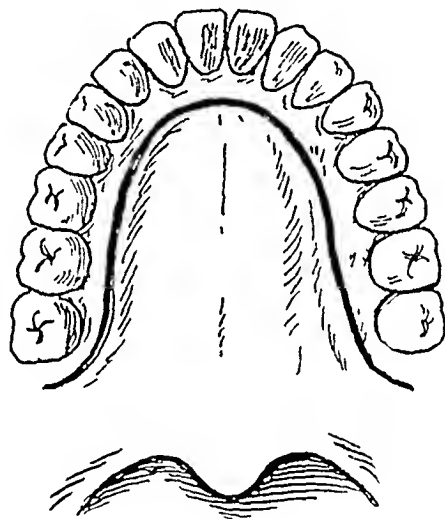


Fig. 60—Incision running parallel with the alveolar margin, and as near to it as possible, to liberate the palatine mucoperiosteum, used in the "push-back-operation."

Guided by past experiences, I felt that many useful suggestions were made by former authorities and forgotten by their successors. This has been the case in practically every surgical subject. Hence a complete survey of the literature on congenital insufficiency of the palate was undertaken, a resume of which appears in the body of this paper.

As outlined in the essay, three methods of treating velopharyngeal insufficiency were employed either alone or in combination.

- 1 The use of prosthetic appliances in the form of obturator-vela
- 2 Operations to produce constriction of the pharyngeal canal
- 3 Operations to lengthen the velum



Most patients with a congenital shortening of the palate cannot tolerate any contrivance within the mouth. Irritation is produced, spasms occur, and alterations in the apparatus must be made constantly to obtain a satisfactory result.

The following methods suggested for the constriction of the pharyngeal canal may be considered:

- 1 Those obtained by cauterization
- 2 Those obtained by plastic operation
- 3 Those obtained by the implantation of tissue or paraffin in the retropharyngeal space

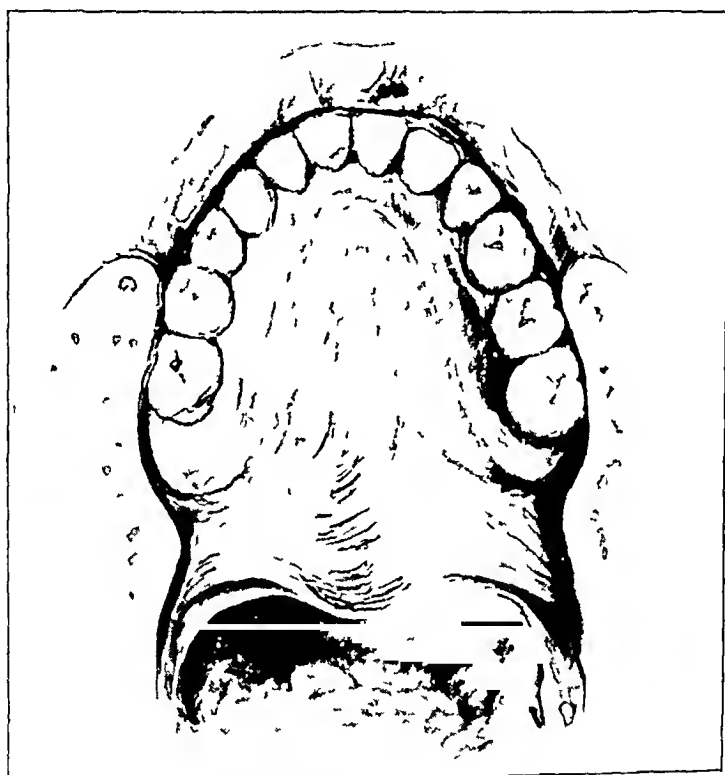


Fig. 61—Artist's presentation of a case of congenital shortening of the palate.

Cauterization can be dismissed as useless, as it produces a marked amount of scar tissue, interferes with the function of the pharynx, disturbs the normal function of the pterygopharyngeus muscle and leads to improper ventilation of the middle ear.

Operations on the pharyngeal wall were condemned because better results can be obtained by methodic speech training, as this causes hypertrophy of the superior constrictor muscle of the pharynx and permits the pterygopharyngeus portion of the superior constrictor muscle to assist the velum in securing velopharyngeal closure.



Fig 62—Artist's presentation of the case in figure 61 with congenital shortening of palate with the mucous membrane removed

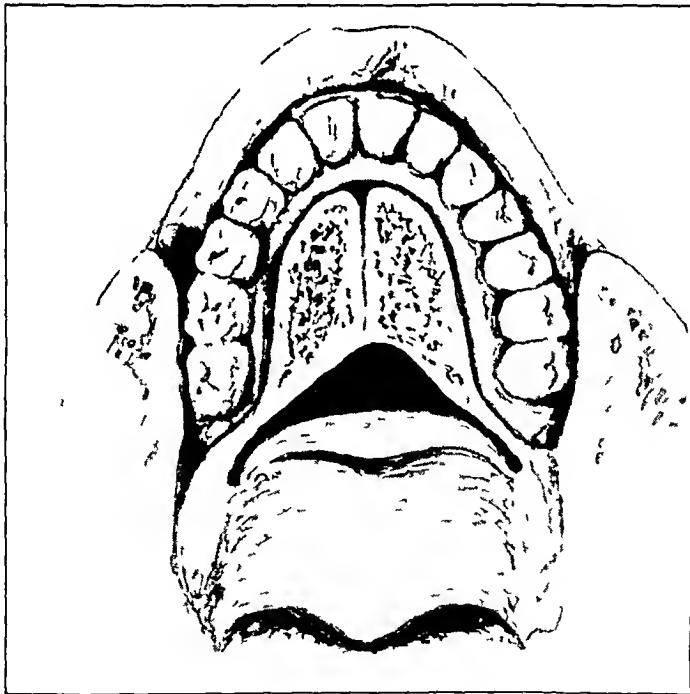


Fig 63—View of case in figure 61 after the mucoperiosteum is elevated and the palate completely freed from its attachment to the palatal processes The fan-shaped portion of the tensor palati muscle is cut

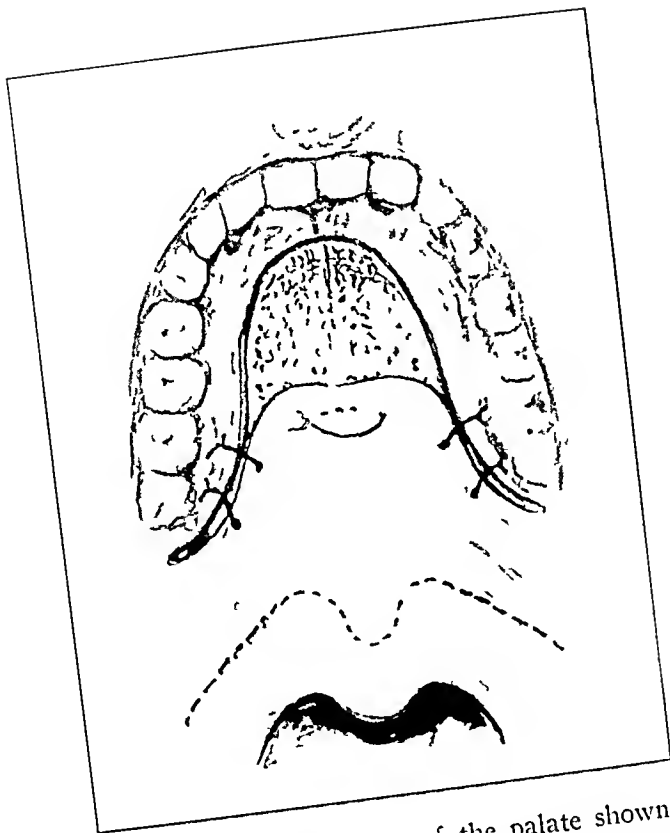


Fig 64—Case of congenital shortening of the palate shown in figure 61 after operation Compare with the original and note the lengthening of the velum secured The dotted line shows position of palate before operation

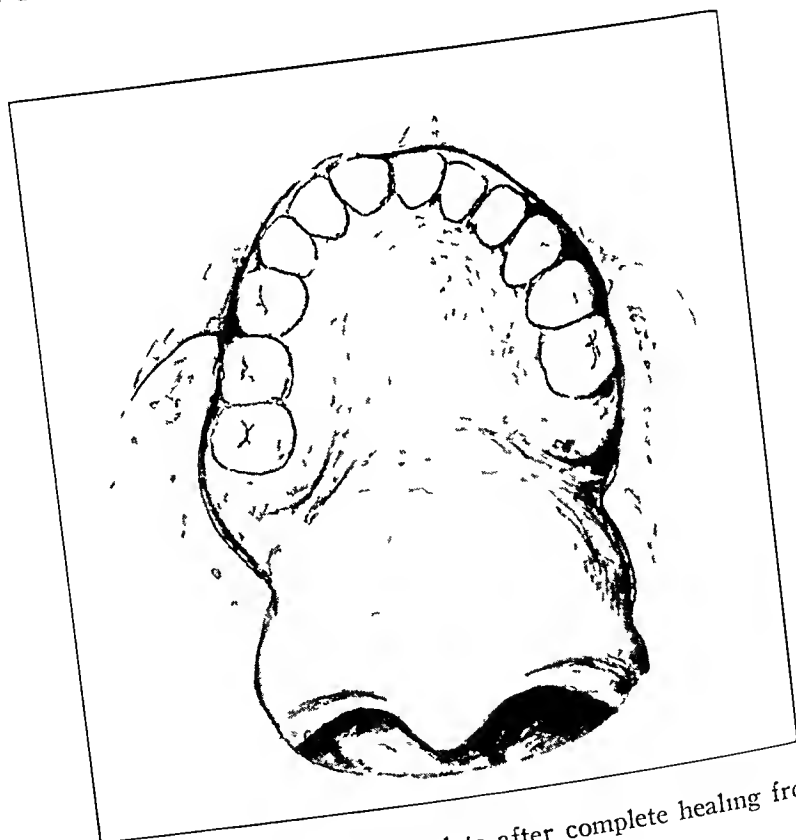


Fig 65—Case of congenital short palate after complete healing from the "push back-operation"

While forward bulging of the pharyngeal wall can be produced by the injection of paraffin or the implantation of fat and fascia into the retropharyngeal space, the first of these methods is so uncertain, as the material injected does not stay in the desired position, and the latter method is fraught with danger which is out of all proportion to the possible benefits to be obtained.

Lengthening of the velum by plastic operations was practically always a failure, since the operators failed to realize that the palatine attachment of the levator palati muscle is placed too far anteriorly and the tensor palati muscle is shorter in all cases of insufficiency of the palate. Hence, it does not make any difference how much the levator palati muscles pull, they cannot possibly bring the velum into its normal position to secure velopharyngeal closure.

While Billroth's method of dividing the hamular process and Agnew's method of cutting the tensor palati muscle relax the tensor palati muscle, these procedures do not change the insertion of the levator palati muscle.

Division of the tensor palati, the palatoglossus and palatopharyngeus muscles as suggested by Meais, does not in any way displace the position of the insertion of the levator palati muscles.

I spent considerable time in the anatomic department working out various methods of lengthening the velum.

On dissecting a specimen with a cleft palate, I realized the important fact that the insertion of the levator palati muscle is placed so far forward that it could not pull the velum against the posterior pharyngeal wall as the normally placed muscle could. Realizing this fact, the solution must be to devise some means of displacing the palate backward so that the levator palati could normally perform this function. I was then struck by the fact that when the elevated palatine mucoperiosteum was completely freed from its attachment to the bony palate the fan-shaped portion of the tendon of the tensor palati which is inserted into the palatine aponeurosis prevented backward displacement of the flap. Division of this fan-shaped portion, along with freeing its attachment to the bony palate, permitted the palate to fall backward by its own weight so that it approximated the pharyngeal wall. This backward displacement of the velum places the levator palati muscles in a position which approaches the normal. I then devised the following operation.

An incision is made as outlined in figure 60. The flap is freed from the bony palate from before backward (fig. 62). Dissection is carried down to the attachment of the palatine aponeurosis at the posterior edge of the bony palate (fig. 63). The posterior palatine arteries are divided in this operation. This constitutes the first stage of the operation. In some cases it has been possible to do the operation

in one stage, when it was felt that the blood supply was adequate. However, as a general rule, the two-stage operation is more satisfactory. The flap is replaced to its original position and the edges sutured. Ten days later, the sutures are removed and the flap raised again. The attachment of the palatine aponeurosis to the bony palate is divided, and that portion of the tendon of the tensor palati muscle which is inserted into this aponeurosis is also divided (fig 64). The flap will now fall backward by its own weight against the posterior wall of the pharynx. The anterior edge of this flap is then sutured to the hard palate and to the soft tissue on either side as illustrated in figure 64. In addition to this, the flap is further supported by placing an appliance on the teeth to support the flap. Silver wire passed around each of the molar teeth may be substituted for the appliance. The denuded surface caused by the posterior displacement of the velum rapidly fills in with granulation tissue (figs 64 and 65). I have used this simple method with success in three cases of congenital insufficiency of the palate and in seven cases of shortened palate in which operation had previously been performed either by myself or by other surgeons, but in which velopharyngeal closure was insufficient. The rationale of this method is based on the principle of surgery that holds elsewhere in the body, that muscles must be placed in as near a normal position as possible, in order to obtain their proper function. My patients have been under observation for a sufficient period of time to note the marked improvement in the functional results obtained by this method. With speech training, they can be made to speak almost perfectly.

This research, then, has solved the problem of correcting congenital insufficiency of the palate.

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# THE COURSE OF THE NERVE FIBERS TRANSMITTING SENSATION OF TASTE \*

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In 1822, Francois Magendie after dividing the trigeminal nerve within the skull in dogs made the following statement "The question of taste, formerly so obscure, no longer presents any difficulty. Physiological experiments and pathological observations have solved it. If the trunk of the fifth nerve is divided in the skull, taste is completely lost, even for sour and bitter substances. This total loss of taste has been noticed in persons in whom the fifth nerve has been compressed or altered." The problem of taste was not, however, to be settled so simply and unequivocally.

As it has been impossible to expose the nerves concerned in the mediation of taste sensations throughout their courses, indirect methods of study, such as the following, have been employed: (1) clinical studies checked by pathologic observations, (2) experiments on animals and (3) postoperative observations on human beings. From the evidence which has accumulated, one theory remains constant: the rôle of the chorda tympani in the transmission of sensations of taste. All observers admit that it does transmit these sensations, but there is no agreement as to the route of the taste fibers in this nerve from the terminal sense organs to the central nucleus.

At the time Magendie performed his experiments, little was known concerning the function of the chorda tympani. A few years before, Bellingeri (1818) described it as the sensory part of the facial nerve and assumed that it transmitted sensations of taste to the brain. The significance of this assumption seemed, however, to have been little appreciated until Claude Bernard, Magendie's successor, made his contributions to the studies of taste. Montault, a pupil of Romberg, and Bernard presented a thesis (1831), in which three cases of facial paralysis accompanied by loss of taste over the anterior two thirds of the tongue were reported. In 1843, Bernard reported four more cases, in which the facial palsy was caused by acute infections and fractures. He noted that the general sensitivity of the side involved was not affected and that taste lost during the paralysis returned with recovery. Section of

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\* Submitted for publication, Nov 26, 1929

\* From the Johns Hopkins Hospital and University

the nerve, earlier performed by Magendie, was repeated by Bernard with a knife especially designed for this purpose by Magendie. After division of both facial nerves intracranially he noted loss of taste similar to that which followed section of the chorda tympani in animals. He believed, however, that the loss was not complete, but that the acuity of taste sensation was markedly lessened.

Bernard must have tested for loss of taste after section of the trigeminal nerves in dogs—an experiment frequently made by him—but there is no mention of any such tests in his protocols. He was particularly interested in the trophic changes that followed section of the fifth nerves and these are frequently mentioned, but curiously enough no mention is made concerning the effect of such division on taste. He accepted the views of Magendie, his preceptor, that the fifth nerve transmitted sensations of taste, and sought to explain alterations in taste following division of the facial nerve as due to lack of "motor control" over the taste buds. He stated, "The chorda tympani should be considered a motor nerve, which by its action upon the papillary lingual tissue regulates and renders instantaneous the transference of a rapid stimulus to the sensory nerve which conducts it to its center." When paralyzed, it affects taste, "not as a nerve of sensation, but by a special inertia of the gustatory organs."

It was not then generally conceded that the chorda tympani played an important rôle in the conduction of sensations of taste. Tests which confirmed this view were shortly to be made. Duchenne (1850) and Blau (1879) took advantage of fistulas of the middle ear to make observations on the function of the chorda tympani. They found that by stimulating the internal wall of the tympanum by irrigations, cauterization and faradic current, they could produce sensations of taste in the anterior two thirds of the tongue, but not in the posterior one third. At times the sensation so produced was sweet, at other times sour, while at still other times a prickly sensation was produced. Blau stated that Troltsch had previously produced much the same sensations by pinching granulations over the chorda tympani on the internal wall of a chronically inflamed middle ear. Since these experiments were made, ample opportunity has been afforded to study the effect on taste of division of the chorda tympani nerve during operations on the mastoid and middle ear.

Guzot and Cazalis (1839) were credited by Luciani, and Biffi and Morganti (1846) by Lussana with discovering that the chorda tympani carries taste sensations from the anterior two thirds of the tongue only and that the glossopharyngeal nerve serves the same function for the posterior one third. As previously stated, however, Montault appears to have called attention to this dual supply several years before (1831).

It is now generally accepted that the chorda tympani conducts all taste fibers from the anterior two thirds of the tongue, but there is no unanimity of opinion as to the path that these fibers pursue from the geniculate ganglion in the facial to their central nucleus. The attempts to determine the course of these fibers may be assigned to three periods which, in a general way, conform to three types of investigation. The first period, one in which animal experimentation predominates, covers the first two thirds of the nineteenth century. This period was dominated by Magendie, Bernard and Schiff. The second period, largely one of clinical and pathologic studies, supplemented now and again by animal experimentation, covers the remaining one third of the nineteenth century. The third period, beginning a few years before the close of the nineteenth century and extending to and including the present time, is concerned with tests on patients in whom the cranial nerves have been divided intentionally for the relief of painful tic or some definite lesion.

Several different pathways of the fibers of the chorda tympani from the geniculate ganglion of the facial nerve to the central nucleus have been proposed. These proposals have been based on experimental, clinical and operative observations.

#### PATHWAY PROPOSED BY SCHIFF

Schiff (1867) made a radical departure from the teachings of Magendie and Bernard. We have already noted that it had been conceded by most observers that the chorda tympani contained all the fibers of taste from the anterior two thirds of the tongue. Schiff made the following experiments:

1. He cut the fifth nerve in animals between the brain stem and the gasserian ganglion and found that the sense of taste was lost. He found that if he cut the facial nerve at the pons, taste was not affected, and therefore concluded that the sensations of taste must pass to the brain through the sensory part of the fifth nerve.

2. He found that when he cut the facial nerve at the geniculate ganglion or distal to it the sense of taste was destroyed, and concluded that these fibers must be deflected to the fifth nerve at the geniculate ganglion.

3. He then cut the third branch of the fifth nerve at the foramen ovale without influencing taste, but found that taste was lost when the second branch of the fifth nerve was divided at the foramen rotundum.

He concluded, therefore, that the fibers of the chorda tympani which carried sensations of taste passed by way of the great superficial petrosal nerve from the geniculate ganglion to the sphenopalatine ganglion, by



way of the second division of the fifth nerve to the gasserian ganglion and then through the sensory root to its central nucleus

The validity of Schiff's experiments and the entire conception of the course of the taste fibers suggested by him were quickly questioned His results also differed markedly from those of Claude Bernard, who found that taste was profoundly changed after intracranial division of the facial nerve

However, some early clinical reports appeared to support Schiff's views Eib reported a case in which the second branch of the fifth nerve was destroyed by a "mass of inflammatory" tissue, Senator

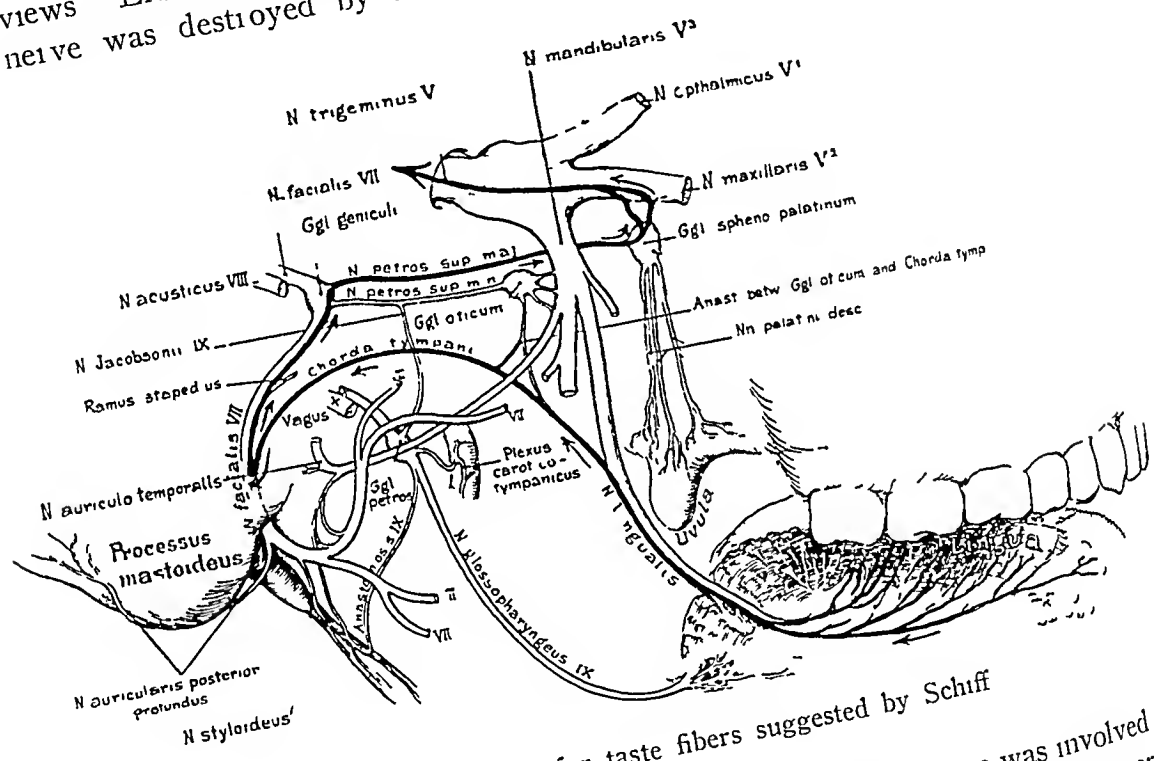


Fig 1.—Pathway for taste fibers suggested by Schiff

(1882) and Salomonsohn (1886), cases in which the nerve was involved in a "chronic inflammatory mass in the middle fossa," and Heusner (1886), another case of the tuberculous caries of the bone (but there was no autopsy) In these cases taste was lost over the anterior two thirds of the tongue These lesions were too diffuse to warrant the conclusions that were made concerning the course of the nerves involved in taste

For a long time, Schiff had considered it probable that not all the taste fibers passed through the chorda tympani, but that part of the fibers at least passed through the lingual He thought, however, that these fibers did not pass directly to the gasserian ganglion, but that they were deflected to the otic ganglion, then to the geniculate by the lesser superficial petrosal nerve and back again to Meckel's ganglion by way

of the great superficial petrosal nerve, and by branches from Meckel's ganglion to the second branch of the trigeminus

#### LUSSANA'S OBSERVATIONS AND PATHWAY PROPOSED BY HIM

Two years after Schiff suggested the route just described, Lussana (1869) made an impressive contribution to the study of the course of the fibers of taste. He assembled a well selected group of clinical cases, and from a study of these arrived at a new conception of the course of taste fibers. He concluded that the nervus intermedius (Wrisberg) was the only nerve which transmitted sensations of taste from the anterior two thirds of the tongue.

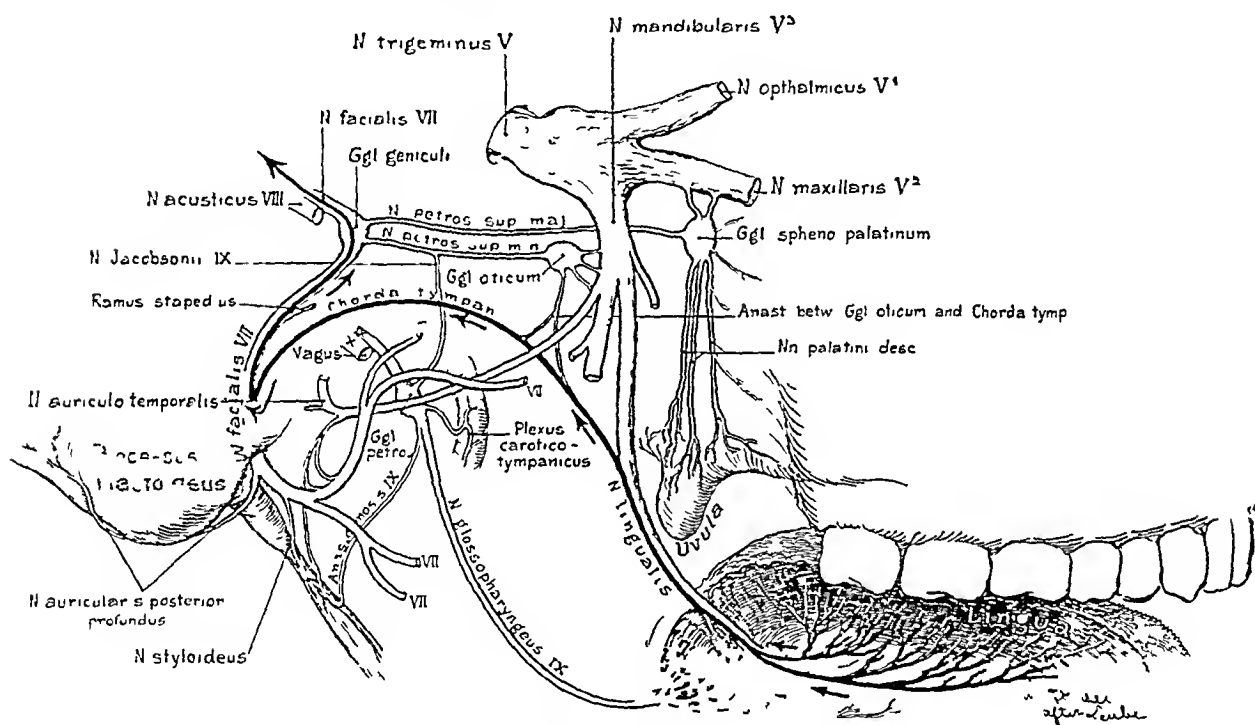


Fig 2—Pathway for taste fibers suggested by Lussana

Lussana's first case was seen with his associate Renzi. The patient had complete loss of sensation over half of the face and tongue (fifth nerve), with no impairment of taste. At autopsy the seventh and eighth nerves were found intact, the fifth destroyed.

His second patient had facial neuralgia. The lingual nerve, including the chorda tympani, had been divided by an operation—"the first time such a procedure had been done in the history of science." Taste was completely lost over the anterior two thirds of the tongue, but pain sense was not affected. This experiment was used by him to eliminate the glossopharyngeal nerve as the nerve of taste for the anterior two thirds of the tongue.

His last and crucial case was again "the only case of its kind in science" In this patient the chorda tympani had been divided, and there had been no injury to the fifth nerve The patient, a man aged 48, had gradually become deaf in one ear, and in seeking relief had fallen into the hands of a charlatan who, in the presence of many onlookers, attempted to demonstrate his skill Three times a long, narrow lance was thrust deeply into the ear The patient fell to the floor in great agony, a convulsion followed and hemiplegia developed The charlatan fled in haste from the angry mob Lussana found this patient two years later The paralysis had cleared, sensation in the face was normal, but taste for the anterior two thirds of the tongue was still lost The chorda tympani had been divided

Lussana supported his unique clinical observations by experiments on animals After cutting the inferior maxillary nerve above the entrance of the chorda tympani into the lingual or intracranially, he found no alteration in taste When the chorda tympani was divided in the tympanum, taste was permanently lost Three years later he published additional data supporting his original contention and referred to the "remarkable" earlier work of Stich (1851), who had collected from the literature many cases of facial paralysis accompanied by loss of taste Lussana's earlier paper provoked much adverse criticism on the part of Schiff, Vulpian and Vizioli

#### PATHWAY SUGGESTED BY ZIEHL

Ziehl (1889) proposed still another pathway, thus adding to the confusion which already existed He too believed that the taste fibers entered the brain by way of the fifth nerve, but thought that they passed by way of the third branch into the gasserian ganglion instead of by the second as Schiff had suggested This course was based on the observations of Romberg, confirmed by autopsy which was "performed by Henle in the presence of Johannes Muller" In this case taste was lost over the anterior two thirds of the tongue on one side, and at autopsy a mass of granulation tissue was found which compressed the third division of the fifth nerve at the foramen ovale Ziehl believed that the observations in this case indicated that sensations of taste were carried to the brain by the third branch of the fifth rather than by the second as thought by Schiff and Erb Accepting the view that all taste fibers pass up the chorda tympani to the geniculate ganglion, he assumed that they then passed by way of the small superficial petrosal nerve directly or by detour through the tympanic plexus, probably in both ways, to the otic ganglion and then by its communicating branches to the third division of the fifth through the gasserian ganglion to the brain

Many of Ziehl's views were based on the none too definite results of animal experiments made by Vulpian, who claimed that taste was lost after the fifth nerve was divided intracranially, but was unaffected when the seventh and ninth were divided within the skull

Ziehl's theory was the one that later become most generally accepted. It received support from a new line of evidence—the effects on taste of operations on the gasserian ganglion performed by Krause. Ziehl's theory also seemed to be supported by a case reported by Ferguson, who found at autopsy in a patient in whom taste to the anterior two thirds of the tongue had been lost, an exostosis which compressed the vidian nerve

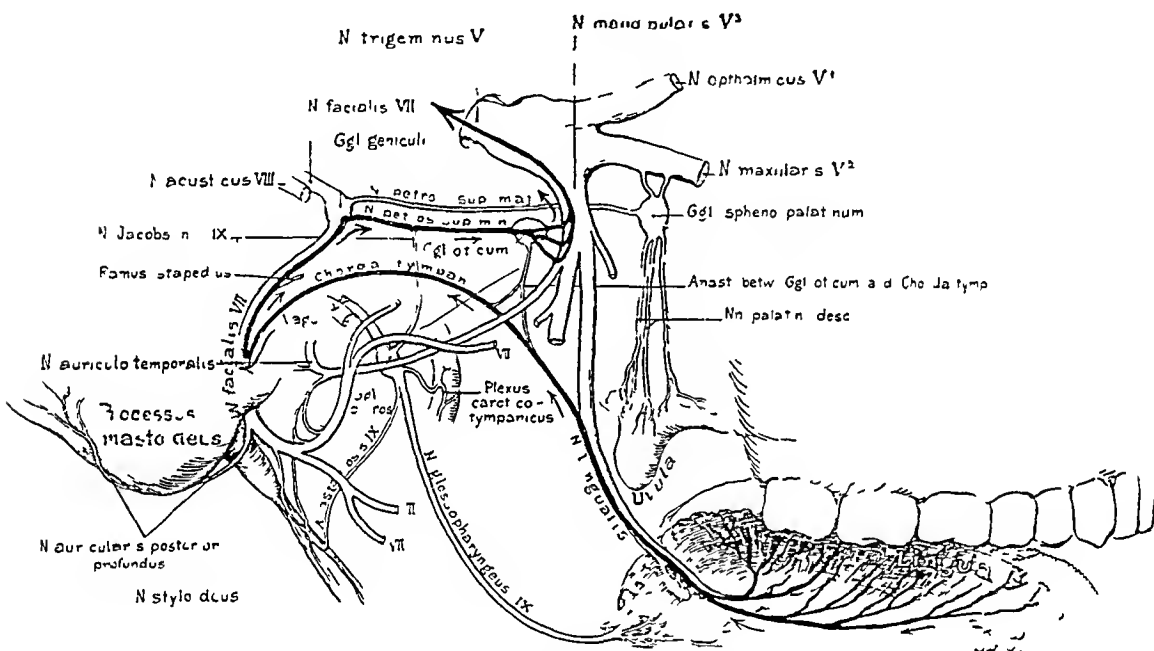


Fig 3—Pathway for taste fibers postulated by Ziehl, and later supported by the operative results of Krause on human subjects

Gowers (1885 and 1897) ardently championed the theory that the fifth nerve was the pathway, without indicating preference for either the second or third branch. He not only accepted the circuitous pathway proposed by Schiff, but, as the result of the examination of three patients in each of whom taste was lost over the entire half of the tongue, was convinced that "taste impressions reach the brain solely by the roots of the fifth nerve and that the doctrine that the roots of the glossopharyngeal nerve had anything to do with taste is a curious myth due to too wide an induction from certain anatomic facts and from dubious experiments on animals." And again "It is possible that nerve fibers for taste on the back of the tongue may be distributed with the

ninth nerve, reaching there from the otic ganglion of the trigeminus by the small petrosal nerve and the tympanic plexus. This course, I confess, seems strangely circuitous, but it is scarcely more circuitous than that which is certainly taken by taste fibers of the front of the tongue." Although Gowers' publications were twelve years apart, his views on taste remained unchanged. However, despite Gowers' standing in the medical world, his claim that the fifth nerve conducted taste fibers from the posterior one third of the tongue gained few supporters. Too many cases were observed which proved that his conclusions were incorrect.

Dixon strongly opposed the views of Gowers and became the outstanding champion of the route through the facial nerve. Dixon's impressions are summed up in the following quotation: "We must remember that we are not forced to accept these complicated courses (for taste innervation) for the geniculate ganglion is the homologue of the spinal ganglia just as is the gasserian of the fifth nerve. The nervus intermedius is considered to be continuous with the chorda tympani and so would represent a continuation of these fibers to the ganglion cells of the brain." He also emphasized the fact that in the human embryo, the chorda tympani is a direct branch of the facial nerve and in the early stages of development is not connected with the lingual nerve.

#### PATHWAY FOR TASTE THROUGH THE GLOSSOPHARYNGEAL NERVE

At least as early as 1834, the glossopharyngeal nerve was considered the nerve of taste for the entire tongue (Lussana). Biffi and Morganti (1846) determined the lingual supply to the anterior two thirds of the tongue and the glossopharyngeal supply to the posterior third. As previously indicated, Montault had already anticipated these observations. Despite the support favoring a fifth or seventh nerve supply for taste, there are those who believe that other evidence indicates that the ninth nerve supplies taste fibers to the entire tongue.

Eulenburg (1871), after obtaining negative results following section of the fifth and seventh nerve in animals, suggested that there must be a communication between the geniculate ganglion and the ninth nerve through the small superficial petrosal nerve, the tympanic plexus and Jacobson's nerve. Landois (1880) also taught that taste was carried by the ninth nerve, possibly by the route suggested by Eulenburg or by a branch passing directly from the facial nerve in the fallopian canal to the ganglion petrosum of the glossopharyngeal nerve.

Lehmann (1884) reported a cerebral injury with paralysis of the ninth nerve and none of the fifth, taste was reported lost over the entire one half of the tongue. Luciani (1915) in his textbook of physiology supported the glossopharyngeal theory. Recently Doyle (1923) cited a case in which taste was lost over one half of the tongue after periph-

eral avulsion of the ninth nerve, but the sensory root of the fifth had previously been avulsed. Although this case is cited to support the glossopharyngeal theory of taste, taste was not tested either before or after division of the trigeminus or before avulsion of the glossopharyngeal nerve. This evidence is therefore inconclusive as far as the anterior two thirds of the tongue is concerned.

It can readily be understood from the foregoing comment that tumors, inflammatory lesions, and cranial injuries have almost always affected more than one nerve and have therefore rendered any conclusions untrustworthy. The results of animal experimentation are so variable that no conclusions can be drawn.

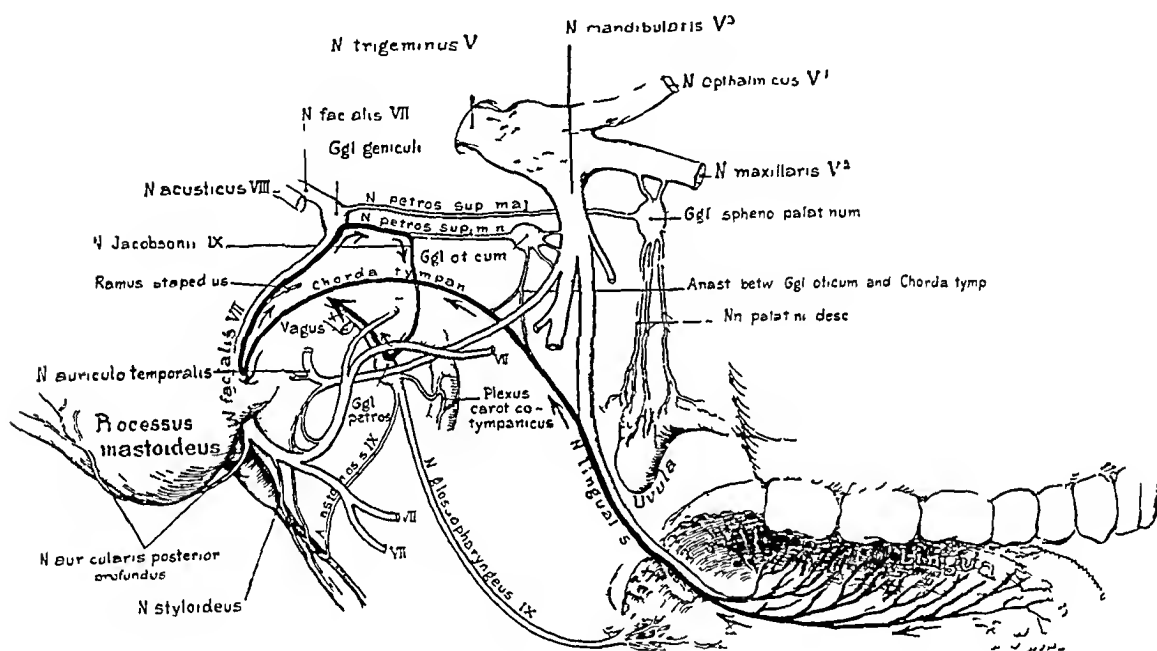


Fig. 4—Pathway for taste fibers suggested by Eulenburg and Landois

#### OPERATIONS ON PATIENTS

With the development of cranial surgery, a better opportunity was afforded to determine the effects on taste of section of the different cranial nerves. Krause (1895) divided intracranially the second division of the fifth nerve. Taste was not affected. Krause's observations did not support the views of Schiff and Erb, for taste was not affected when the great superficial petrosal and vidian nerves and the branches of the sphenopalatine ganglion were divided. Later the ganglion was removed from the same patient, and taste was lost. It seems natural, therefore, that Krause should have concluded that the third branch of the fifth conducted the fibers of taste.

Krause's work was quickly criticised by Dixon, who believed that the results were due to injury of the geniculate ganglion when the dura was stripped from the floor of the middle fossa. Dixon believed that both petrosal nerves might be stripped from their bed during exposure of the ganglion and that this ganglion might be pulled on or injured. Weakness of the facial muscles, even paralysis of these muscles in Krause's cases, seemed to support this contention.

Other surgeons began to report cases but with varying conclusions. Tiffany (1894) reported loss of taste after division of the second and third branches of the fifth nerve. Finney and Thomas reported loss of taste after extirpation of the ganglion in one case, in another, taste was preserved. Gowers cited the observations made on five patients operated on by Sir Victor Horsley and Ballance. Taste was lost in four and preserved in one. Horsley's results and views were much like those of Krause. Cushing in 1903 reported twenty cases of operation on the gasserian ganglion. In four, taste was impaired. Davies (1907) added twenty cases, the results almost duplicating those of Cushing. Taste was lost in one case, impaired in three and unchanged in sixteen. Krause later reported six cases, taste being lost in two, impaired in three and unchanged in one. Krause finally came to the conclusion, because of the variable observations, that taste fibers must pursue different courses in different individuals, and Oppenheim, Germany's leading neurologist at that time, concurred in this view. Harris (1926) published a series of eighty-six cases of tic douloureux in which alcohol had been injected into the third division of the fifth nerve or the gasserian ganglion. Taste was lost in eighty of these. Such an injection probably produces a more localized lesion than operations on the gasserian ganglion when approached in the usual way through the middle fossa. He was surprised to find, as were others before him, that although in a few cases taste was totally lost at first, it sometimes returned later, even when the tongue remained anesthetic. The objection can no longer be raised in these cases that the geniculate ganglion was injured in stripping the dura from the middle fossa. Harris, like Krause, expressed the belief that taste fibers have different courses in different persons, but that the fifth nerve is the principal nerve of taste. In explanation of these differences he cited the work of Nageotte, in which it was shown that the fifth and sensory parts of the seventh and ninth nerves have a common nucleus which is continuous caudalward.

#### MATERIAL OF PRESENT STUDY

We have presumed to add to the lengthy literature on the course of taste fibers because we have material which has hitherto been unavailable. Pure isolated divisions of the fifth, seventh and ninth nerves have been

performed subtentorially for the relief of surgical conditions. Combined division of the fifth and seventh has also been performed. The fifth nerve has been divided intracranially at the pons for trigeminal neuralgia. The subtentorial operation has the advantage of not disturbing the petrosal nerves or geniculate ganglion or any other cranial nerve. Division of the seventh nerve alone has occurred during the removal of tumors of the cerebellopontine angle in a method recently described. As yet it has been impossible to extirpate these tumors without dividing the seventh nerve. As the fifth and ninth nerves are usually pushed aside by these tumors, they may not be injured when the tumor is removed. There is also an instance of a pure lesion of the seventh nerve which was accidentally injured when the auditory nerve was divided for relief from Meniere's disease. There was no disturbance of the fifth or ninth nerve in this case.

#### NECESSITY OF CONTROL OBSERVATIONS

Before presenting our evidence concerning the course of taste fibers derived from cases in which pure isolated lesions have been produced, it may be well to state something concerning (1) the methods of testing taste and (2) the necessity of making control tests. An appreciation of these two things may explain to some extent the divergent views held by different observers.

For a long time we were unable to understand why members of our own staff obtained different results. Three examiners would obtain results as variable as those reported in the literature. Even in a patient whose taste was found to be lost by one examiner, normal or subnormal taste would be found by another. Different results may be obtained for the following reasons: 1. Patients confuse touch and taste. 2. When patients are allowed to withdraw the tongue, taste will quickly be perceived by oral and posterior glossal taste buds. 3. At times, saliva coming in contact with the solution would carry the substance to be tested to the back of the mouth. 4. Patients are prone to guess, particularly when sensation is present. 5. By the sense of smell, patients may tell before tasting whether the solutions offered them are acid or bitter, solutions should therefore be used which do not stimulate smell.

In testing taste, the tip of the tongue should be covered with gauze and held by the examiner until the taste has been accurately identified in one of two ways: (1) The patient points to one of four tastes printed on a card, or (2) he nods when the examiner mentions the taste. The tongue is not to be drawn into the mouth until the taste has been definitely determined. If this method of examination is employed, the results will be accurate and uniform. Preoperative observations should be made as control experiments. Deviations from the normal occur



frequently and either unilaterally or bilaterally. Therefore unless taste is carefully tested before the operation, erroneous conclusions may be drawn. The acuity of taste varies considerably in different patients, as is indicated by the following observations.

CASES 1 and 2—Two patients, both men, suffered with *tic douloureux*. Examination showed that neither had taste perception over the anterior two thirds of the tongue on either side when tested before operation.

CASE 3—A man, aged 40, had a painful malignant ulcer of the tongue. He had no taste perception over the anterior two thirds of the tongue (either side) when tested before the operation.

CASE 4—A man, aged 56, had had the gasserian ganglion removed seven years by the temporal route before the test was made. This patient had no sensation of taste on the anterior two thirds of the tongue on either side.

CASE 5—A man, aged 65, entered the hospital for treatment for *tic douloureux*. When tested for taste perception before operation, it was found to be absent on the side of the neuralgia, but normal on the other side (anterior two-thirds). No cause for loss of taste on the affected side could be determined.

CASE 6 and 7—A man, aged 49, and a woman, aged 62, were afflicted with *tic douloureux*. Before operation neither sugar nor salt could be detected on either side of the tongue (anterior two-thirds). Acid and bitter substances could be tasted, but perception was delayed.

CASE 8—A woman, aged 45, was afflicted with *tic douloureux*. She could not taste sweet or bitter substances. She could taste sour substances after thirteen seconds and salt after twenty-three seconds. The observations on both sides were identical.

CASE 9—A man, aged 60, with *tic douloureux* could not taste sugar, salt or bitter substances on either side of the tongue (anterior two-thirds). Sour substances could be tasted after eight seconds.

CASE 10—A man, aged 63, afflicted with *tic douloureux* could not taste sugar or bitter substances. Perception of salt and sour were present but were delayed eight seconds.

It will be seen from the observations given that it cannot be assumed that taste is normal in any person. Each one should be tested before operation, for the incidence of defective taste is high and the character of the change is variable. Although loss or diminution in acuity of taste is usually symmetrical, this is not necessarily so, as is indicated by the hemigeusia in case 5. Had not taste been tested before operation in this case, section of the sensory root of the fifth nerve would have been regarded as the cause of the loss of taste.

There is still another possible cause of error. If alcoholic solutions of bitter substances are used diffusion occurs, and after a minute or more, taste may be perceived on the other side. The patient may or may not know on which side the taste perception occurs.

In all of our observations one minute has been the upper limit for taste determinations. Substances not detected within this time will not be appreciated at all.

## PURE EXPERIMENTAL NERVE LESIONS

The material has been grouped under the following headings (1) pure fifth nerve lesions, (2) pure ninth nerve lesions, (3) combined pure fifth and ninth nerve lesions, (4) pure seventh nerve lesions (intracranial) and (5) pure seventh nerve lesions (peripheral)

## GROUP I PURE FIFTH NERVE LESIONS

CASE 1—A sparsely nourished woman, aged 63, sought relief from trigeminal neuralgia. Pain like a pin prick began eleven years before examination, in the right side of the face below the eye. At first the attacks were not severe, but gradually they became more so and occurred more frequently, six years before, they became excruciating. They were induced by eating, drinking or touching the lip. Four injections of alcohol afforded relief over varying periods of time. The neurologic examination gave entirely negative results. Gustatory tests were not made before operation.

On Sept. 17, 1927, the right sensory root was divided by the subcerebellar route. Total anesthesia resulted for all forms of sensation in the domain of the trigeminal nerve.

Five months after operation, the results obtained by one of us (W. E. D.) in tests for taste were

	Right (Affected Side), Seconds	Left Side
Salt	0	40 seconds
Acid	15	Instantly
Bitter	10	5 seconds
Sugar	0	0 seconds

CASE 2—A rather obese woman, aged 70, sought relief for *tic douloureux* on the right side. Two years before consulting us she experienced sudden attacks of sharp pain, like needle pricks, in the right molar region. The pains became progressively more severe and more frequent. Gradually also the involved area of the face spread to the eye and the forehead. Eating, drinking, cold and touching the face precipitated the pain. The physical and neurologic examinations gave entirely negative results. Gustatory tests were not made before operation.

On March 30, 1927, the sensory root of the right trigeminal nerve was divided at the pons, by the subcerebellar route. Complete anesthesia for all forms of sensation followed in the domain of the trigeminal nerve.

Eight days after operation, the following results were obtained by one of us (W. E. D.) in a test for taste

	Right (Affected Side), Seconds	Left
Sugar	15	Instantly
Salt	50	Instantly
Acid	20	Instantly
Bitter	60	Instantly

Eleven days after operation, the following results were obtained by another examiner

	Right (Affected Side), Seconds	Left
Sugar	0	Instantly
Salt	0	Instantly
Acid	20	Instantly
Bitter	3	Instantly

Nine months after operation, the following results were obtained

	Right (Affected Side), Seconds	Left, Seconds
Sugar	0	0
Salt	0	0
Acid	2	2
Bitter	2	2

The results of a recent test, two and one-half years after operation were

	Right (Affected Side), Seconds	Left, Seconds
Sugar	0	30
Salt	2	2
Acid	2	1
Bitter	2	2

CASE 3—A slender, emaciated woman, aged 51, was referred by Dr John Gilmore, of Wheeling, W Va, for relief from tic douloureux. Ten years ago a slight pain began in the lower teeth and the lower lip on the left side, without known cause. Gradually the pain became more severe and spread to the upper two branches of the nerve, thus involving the entire area of the right trigeminal nerve. The pain was paroxysmal and of terrific intensity. A draught of cold air, eating and drinking induced the attacks. All of the teeth on the left side had been extracted in a futile effort to abolish the pain. She had lost a great deal of weight because eating was painful. Physical and neurologic examinations yielded negative results. Section of the left sensory root of the trigeminal nerve at the pons (sub cerebellar route) was performed on Feb 7, 1928. Total anesthesia for all forms of sensation resulted in the domain of the affected nerve.

Before operation the following results were obtained by an associate in a test for taste on the affected side only

	Left (Affected Side)
Sugar	7 seconds
Salt	15 seconds
Acid	8 seconds
Bitter	Not identified, called "sweetish"

Three days after operation, the following results were obtained by one of us (W E D)

	Left (Affected Side), Seconds	Right, Seconds
Sugar	10	10
Salt	0	2
Acid	10	2
Bitter	10	2

Ten days after operation, the following results were obtained by an associate

	Left (Affected Side), Seconds	Right, Seconds
Sugar	5	5
Salt	20	10
Acid	18	10
Bitter	15	12

CASE 4—A large robust man, aged 42, was referred by Dr John Gilmore, of Wheeling, W Va, for treatment for tic douloureux Six years before, tenderness was first noticed along the lower branch of the trigeminal nerve Paroxysms of pain soon developed at the site of tenderness The pain gradually increased in severity, and finally it involved all three branches of the nerve, though the starting point was in the mandibular branch Never a day passed without several attacks of terrific pain Eating, drinking and touching the face induced the pain Physical and neurologic examinations gave entirely negative results

On Feb 7, 1928, the sensory root of the left trigeminal nerve was sectioned totally at the pons Complete anesthesia over the domain of this nerve resulted

Before operation the results of a gustatory examination on the affected side only, made by an associate, were as follows

	Left (Affected Side)
Sugar	10 seconds
Salt	12 seconds
Acid	20 seconds
Bitter	15 seconds

Seven days after operation, the following results were obtained by one of us (W E D)

	Left (Affected Side), Seconds	Right, Seconds
Sugar	30	20
Salt	Not recognized	5
Acid	2	2
Bitter	2	2

Ten days after operation, the following results were obtained by an associate

	Left (Affected Side), Seconds	Right, Seconds
Sugar	25	15
Salt	12	5
Acid	5	7
Bitter	20	10

CASE 5—A well nourished woman aged 59 was referred by Dr H Klinzing, of Pittsburgh, for treatment for pain in the right side of the face Fifteen years before she was seen by us the type of pain of which she complained began in the

right temple, soon passed to the eye, where it became more intense, and persisted for about twelve hours. There was some radiation of the pain to the upper and lower teeth on the same side, also to the back of the head and ear on the right side. The pain never spread to the left side, nor did it ever arise there. It was present almost every day and generally lasted about twelve hours. It usually began about 4 o'clock in the afternoon. Acetylsalicylic acid and a brand of amidopyrine relieved the patient only partially and for about two hours. Eating, drinking and rubbing the face did not induce the pain nor did anything else of which she knew. Physical and neurologic examinations yielded entirely negative results.

Because of the radiation of the pain to the teeth, a diagnosis of an unusual form of trigeminal neuralgia was made.

Complete section of the right sensory root at the pons was performed on July 28, 1927. Total anesthesia resulted for all forms of sensation in the affected nerve. Complete section of the sensory root was made because of the unusual type. There has not been a suggestion of the former pain to the time of this writing, two years later.

Before operation, the following results were obtained by an associate in examinations for taste:

	Right (Affected Side)	Left
Sugar	Instantly	Instantly
Salt	Instantly	Instantly
Acid	Instantly	Instantly
Bitter	Instantly	Instantly

Seven days after operation the following results were obtained by the same associate:

	Right (Affected Side), Seconds	Left
Sugar	2	2
Salt	2	Instantly
Acid	2	Instantly
Bitter	Instantly	Instantly

CASE 6—A well nourished woman, aged 48, was referred by Dr. Louis Hamman. Her complaint was attacks of pain in the right eye. Since the age of 15, the patient had had occipital headaches extending to the vertex. About nine years before she consulted us this headache seemed to change to a single pain localized in the right eyeball. At first the pain occurred about every six weeks. Gradually it increased to once a week and became much more intense. It began gradually, at first being scarcely perceptible, it continued steadily to become more severe, reaching its maximum intensity in about twelve hours, and then gradually subsided. Each attack lasted about forty-eight hours. Codeine deadened the pain slightly. There was no pain in the face. Nothing induced the pain or modified the attack. At times there was a sensation of cold in the eyeball. The pain did not radiate to any part of the sensory domain of the trigeminal nerve. There was no known history of similar pain in any member of her family. The results of physical and neurologic examinations were normal.

The pain was suggestive of migraine. Relief from pain of seemingly similar character had been given by section of the sensory root in three other cases; this operation was performed on the right side on July 9, 1929. Total anesthesia resulted for all forms of sensation in the right terminal area.

Before operation, taste was found by an associate to be normal on both sides

After operation (eight days), the following results were obtained by an associate

	Right (Affected Side), Seconds	Left, Seconds
Sugar	3	2
Salt	2	2
Acid	2	2
Bitter	2	2

CASE 7—A sparely nourished man, aged 58, was referred by Dr Le Grand Guerry, of Columbia, S C, because of bilateral tic douloureux. For twenty-one years he had suffered with trigeminal neuralgia of the right side, apparently all three branches were involved at the onset. The left side became involved six years before we saw him, but only the second and third branches were painful. The pains on both sides had all the characteristics of tic douloureux. They were paroxysmal, and were brought on by eating, drinking, cold air or touching the face. He had had numerous peripheral operations and injections of alcohol, with short periods of temporary relief. Usually when the pain began on one side (either side) it spread to the other side, though there were periods when the attacks affected one side only.

The diagnosis was bilateral trigeminal neuralgia.

On April 30, 1926, both the right and left sensory roots of the trigeminal nerves were sectioned at the pons (subcerebellar route) at the same operation.

Tests for taste were not made before operation. Three weeks after operation, the patient could promptly taste sweet, salt, acid and bitter on both sides. The time of recognition of the taste was not noted, as this was our first test of this function. Six months later, he wrote: "The taste is perfect, so I can't understand why I am not gaining faster the sense of feeling or touch inside the mouth."

After the operation, both sides of the face were completely anesthetic to all forms of sensation.

CASE 8—A sparely nourished woman, aged 62, was referred for typical right-sided neuralgia of three years' duration. For over a year, the pains were only occasional and of very short duration, gradually, they became more frequent, of longer duration and more intense. Finally, each paroxysm of pain lasted about three minutes. They were induced by eating, drinking, cold air or touching the face. They began over the right eye and did not spread.

Physical and neurologic examinations gave entirely negative results.

The sensory root of the right trigeminal nerve was sectioned at the pons on Dec 21, 1928. There was complete loss of all forms of sensation in the domain of the right trigeminal nerve after the operation.

Examination for taste was not made before or immediately after operation.

Seven months after the operation, the following results were obtained in tests for taste by one of us (W E D)

	Right (Affected Side), Seconds	Left, Seconds
Sugar	1	4
Salt	1	40
Acid	1	40
Bitter	12	45

All forms of taste were much less intense on the left (normal) side.

TABLE 1 (Group I) —Results of Examinations for Taste, Over the Anterior Two Thirds of the Tongue, After Section of the Sensory Root of Trigeminal Nerve at the Pons, in Every Instance Total Anesthesia for all Forms of Sensation, Has Followed in the Affected Trigeminal Domain, These Cases Are Therefore Cases of Pure Fifth Nerve Lesions

Patient	Age	Diagnosis	Operation	Time of Test	Results of Sensory Examination Over Trigeminal Area	Time of Taste Perception		Control Tests (Before Operation)	
						Affected Side	Normal Side	Affected Side	Normal Side
F (Case 1)	63	Trigeminal neuralgia	Section of sensory root (cerebellar route)	5 months after operation	Total anesthesia to all forms of sensation	Sugar 0	0	No tests before operation	No tests before operation
						Salt 13 seconds	40 seconds	No tests before operation	No tests before operation
						Bitter 10 seconds	Instantly	No tests before operation	No tests before operation
						Sugar 15 seconds	Instantly	No tests before operation	No tests before operation
						Salt 50 seconds	Instantly	No tests before operation	No tests before operation
F (Case 2)	70	Trigeminal neuralgia	Section of sensory root (cerebellar route)	8 days after operation	Total anesthesia to all forms of sensation	Acid 20 seconds	Instantly	No tests before operation	No tests before operation
						Bitter 60 seconds	Instantly	No tests before operation	No tests before operation
						Sugar 0	Instantly	No tests before operation	No tests before operation
						Salt 0	Instantly	No tests before operation	No tests before operation
						Acid 20 seconds	Instantly	No tests before operation	No tests before operation
						Bitter 3 seconds	Instantly	No tests before operation	No tests before operation
						Sugar 0	0	No tests before operation	No tests before operation
						Salt 0	0	No tests before operation	No tests before operation
						Acid 2 seconds	2 seconds	No tests before operation	No tests before operation
						Bitter 2 seconds	30 seconds	No tests before operation	No tests before operation
F (Case 3)	51	Trigeminal neuralgia	Section of sensory root (cerebellar route)	9 months after operation	Total anesthesia to all forms of sensation	Bitter 0	2 seconds	No tests before operation	No tests before operation
						Sugar 0	2 seconds	No tests before operation	No tests before operation
						Salt 2 seconds	2 seconds	No tests before operation	No tests before operation
						Acid 2 seconds	30 seconds	No tests before operation	No tests before operation
						Bitter 2 seconds	2 seconds	No tests before operation	No tests before operation
						Sugar 2 seconds	1 second	No tests before operation	No tests before operation
						Salt 2 seconds	2 seconds	No tests before operation	No tests before operation
						Acid 2 seconds	10 seconds	No tests before operation	No tests before operation
						Bitter 10 seconds	2 seconds	No tests before operation	No tests before operation
						Sugar 0	2 seconds	No tests before operation	No tests before operation
M (Case 4)	42	Trigeminal neuralgia	Section of sensory root (cerebellar route)	3 days after operation	Total anesthesia to all forms of sensation	Salt 10 seconds	10 seconds	No tests before operation	No tests before operation
						Acid 10 seconds	10 seconds	No tests before operation	No tests before operation
						Bitter 5 seconds	10 seconds	No tests before operation	No tests before operation
						Sugar 20 seconds	10 seconds	No tests before operation	No tests before operation
						Salt 18 seconds	12 seconds	No tests before operation	No tests before operation
						Acid 15 seconds	20 seconds	No tests before operation	No tests before operation
						Bitter 30 seconds	1 seconds	No tests before operation	No tests before operation
						Sugar 0	2 seconds	No tests before operation	No tests before operation
						Salt 2 seconds	2 seconds	No tests before operation	No tests before operation
						Acid 25 seconds	15 seconds	No tests before operation	No tests before operation
F (Case 5)	59	Trigeminal neuralgia	Section of sensory root (cerebellar route)	7 days after operation	Total anesthesia to all forms of sensation	Bitter 12 seconds	7 seconds	No tests before operation	No tests before operation
						Sugar 5 seconds	10 seconds	No tests before operation	No tests before operation
						Salt 20 seconds	10 seconds	No tests before operation	No tests before operation
						Acid 15 seconds	12 seconds	No tests before operation	No tests before operation
						Bitter 30 seconds	20 seconds	No tests before operation	No tests before operation
						Sugar 0	1 seconds	No tests before operation	No tests before operation
						Salt 2 seconds	2 seconds	No tests before operation	No tests before operation
						Acid 25 seconds	15 seconds	No tests before operation	No tests before operation
						Bitter 12 seconds	7 seconds	No tests before operation	No tests before operation
						Sugar 5 seconds	10 seconds	No tests before operation	No tests before operation
F (Case 6)	48	Migraine-like pain in right eye	Section of sensory root (cerebellar route)	7 days after operation	Total anesthesia to all forms of sensation	Acid 20 seconds	2 seconds	No tests before operation	No tests before operation
						Bitter 2 seconds	Instantly	No tests before operation	No tests before operation
						Sugar 2 seconds	Instantly	No tests before operation	No tests before operation
						Salt 2 seconds	Instantly	No tests before operation	No tests before operation
						Acid 1 instantly	2 seconds	No tests before operation	No tests before operation
						Bitter 3 seconds	2 seconds	No tests before operation	No tests before operation
						Sugar 2 seconds	2 seconds	No tests before operation	No tests before operation
						Salt 2 seconds	2 seconds	No tests before operation	No tests before operation
						Acid 2 seconds	Promptly recognized	No tests before operation	No tests before operation
						Bitter 2 seconds	Instantly	No tests before operation	No tests before operation
M (Case 7)	58	Bilateral trigeminal neuralgia	Section of both sensory roots (cerebellar route)	21 days after operation	Total anesthesia to all forms of sensation	Sugar 0	1 second	No tests before operation	No tests before operation
						Salt 1 second	10 seconds	No tests before operation	No tests before operation
						Acid 1 second	10 seconds	No tests before operation	No tests before operation
						Bitter 1 second	10 seconds	No tests before operation	No tests before operation
						Sugar 1 second	10 seconds	No tests before operation	No tests before operation
						Salt 1 second	10 seconds	No tests before operation	No tests before operation
						Acid 1 second	10 seconds	No tests before operation	No tests before operation
						Bitter 1 second	10 seconds	No tests before operation	No tests before operation
						Sugar 1 second	10 seconds	No tests before operation	No tests before operation
						Salt 1 second	10 seconds	No tests before operation	No tests before operation

*Summary*—In this group are included only those patients in whom total anesthesia for all forms of sensation except taste followed section of the sensory root of the trigeminal. There was essentially no difference in the acuity of taste after division of the sensory root. It may well be asked why these results should be different from those obtained by section of the sensory root by the temporal route as performed by Krause, Cushing and others. By the temporal route the petrosal nerves are torn and at times the geniculate ganglion is injured in stripping the dura from the temporal bone. Since the petrosal nerves have been included in the pathways of taste, their injury adds a complication and prevents the results from being accepted as pure fifth nerve lesions. By the sub-cerebellar route, which we have used exclusively, the lesion is strictly that of the fifth nerve, for no other nerves cross the line of approach.

Twenty-five additional cases of presumably total trigeminal section by this route are not included in this group because sensation in varying degrees has been retained. The preservation of sensation is not due, as might well be reasoned, to subtotal section of the sensory root but to variable adjacent accessory fibers which retain the sensory function. In none of these additional cases has taste been lost after partial or total section of the sensory root. Nor is a still greater number of cases of deliberate partial section of the sensory root included, although the results obtained are precisely similar.

Partial section of the nerve is now used exclusively instead of total division, for pain fibers have been found to be located solely in the posterior border of the sensory root and sensation to the face can be left almost intact by preservation of the anterior half of the root.

Perhaps the most impressive test of the series (group 1) that taste is not carried by the trigeminal nerve is offered in case 7, in which the sensory roots of both trigeminal nerves were totally divided at the same operation. Although all sensation of both trigeminal nerves was totally abolished, all forms of taste to the anterior two thirds of the tongue were promptly recognized.

#### GROUP II PURE NINTH NERVE LESIONS

CASE 1—A robust man, aged 45, sought relief for agonizing paroxysmal pains beginning in the tonsil region. These pains were brought on by swallowing and talking, and even occurred spontaneously. The pain was so terrific that he sat in terror, afraid to eat or drink, and held his head inclined at an angle so that the saliva could drool from his mouth on the unaffected side. These pains had been present for three years, though there were periods lasting for months in which the same stimuli would not produce the attacks. He said the pain felt as though a red hot poker were being thrust into the back of the tongue. He had learned that relief could be obtained by the application of cocaine to the affected jaw.

Physical and neurologic examinations gave entirely negative results. The history was typical of glossopharyngeal neuralgia.



On April 6, 1927, the glossopharyngeal nerve was divided intracranially under local anesthesia. Following the operation there was loss of sensation in the back of the tongue and the mouth on the affected side, this extended to the epiglottis below and to the roof of the pharynx above. There was also loss of taste in the posterior third of the tongue. The functions of the other cranial nerves remained entirely normal. A pure ninth nerve lesion was thus produced.

Test for taste by one of us (W E D) on the anterior two thirds of the tongue, ten days after the operation, gave the following results:

	Left (Affected Side), Seconds	Right
Sugar	Instantly	Instantly
Salt	Instantly	Instantly
Acid	Instantly	Instantly
Bitter	Instantly	Instantly

CASE 2—A well nourished man, aged 56, pale and sallow from lack of recent nourishment, was referred by our associate, Dr S J Crowe, for relief from pain that was characteristic of glossopharyngeal tic douloureux. Fifteen years before he was seen by us, while he was talking with a friend, there suddenly appeared an excruciating pain in a well localized spot in the back of the tongue and near the tonsils, it lasted only a few seconds. During the succeeding years, similar momentary pains struck him from time to time, they were so infrequent as not to be a severe handicap. The pain felt as though a red hot iron were being jabbed into the tongue. At first he was unable to discover any inciting cause, but later at certain times the attacks were brought on by eating, drinking and talking. For two weeks before entering the hospital the attacks had been almost continuous, and the patient did not dare to eat, drink or talk, sneezing or coughing also brought on the paroxysms.

Neurologic and physical examinations gave entirely negative results.

On May 11, 1927, under local anesthesia, the glossopharyngeal nerve was divided intracranially. There was loss of sensation over the same area as in the preceding case, and the same loss of taste in the posterior third of the tongue.

One week after the operation, the following results were obtained by one of us (W E D):

	Left (Affected Side), Seconds	Right
Sugar	1	Instantly
Salt	1	Instantly
Acid	1	Instantly
Bitter	1	Instantly

At recent examination there was just an appreciable difference between the time of perception of taste, and to the patient there was also a slight difference in intensity of taste perception. Sensation over the domain of the fifth nerve was entirely normal.

CASE 3—A large, strong, colored man, aged 32, complained of a constant severe pain in the left side of the neck and ear. Four years before this examination a peculiar sensation developed in the left ear, at first it felt as if it were a bug and then a trigger zone in the external auditory canal. He was treated in the Johns Hopkins Dispensary for two years, at which time a swelling was found in the auditory canal.

During the first few months there was some discharge of pus, but later although the swelling was incised on several occasions, it did not continue to drain.

pus The canal became occluded by a hard growth which was tender From this, deafness and ringing in the ear developed Two and one-half years ago a mastoid operation was performed, but no infection was found A mass of fibrous and fatty tissue covered with epithelium was removed from the cartilaginous canal Following this operation, hearing returned and there was relief from pain for over a year One year ago, the present type of pain began, it gradually became worse so that he was unable to sleep at night without taking sedatives The pain was continuous It began in front of the ear, ran back of the ear and down the neck to the angle of the jaw It was aggravated by swallowing cold air and by moving the jaw

Physical and neurologic examinations showed nothing other than a localized lesion in the ear The distribution of pain made us feel that the glossopharyngeal nerve was affected

On Feb 18, 1928, the left glossopharyngeal nerve was divided intracranially No other nerves were injured Before operation the following results were obtained by an associate in an examination for taste

	Left (Affected Side), Seconds	Right, Seconds
Sugar	10	10
Salt	12	10
Acid	5	7
Bitter	5	5

Eight days after the operation, the following results were obtained by the same associate

	Left (Affected Side), Seconds	Right, Seconds
Sugar	3	3
Salt	7	8
Acid	10	5
Bitter	4	3

*Summary*—In these three cases of total section of the glossopharyngeal nerve, taste remained normal over the anterior two thirds of the tongue on the affected side There can be no purer nerve lesions than those produced by intracranial section of the glossopharyngeal nerve, for no other nerves are touched during exposure and section of the nerve The results of this group should, therefore, dispose of the ninth nerve as a conductor of taste from the anterior two thirds of the tongue

### GROUP III COMBINED PURE FIFTH AND NINTH NERVE LESIONS

A large, somewhat undernourished man aged 69, complained of severe facial pain caused by carcinoma of the left side of the face The growth which was of eleven years' duration, was first observed just within the left auditory canal It had been treated with radium for the past eight years It had healed and reopened on several occasions The pain began two weeks after treatment with "radium seeds" at another clinic two years before It had steadily become worse At times the whole side of the face pained Associated with the carcinoma there was necrosis of the neck of the mandible from which the open sinus persisted

TABLE 2 (Group II)—Results of Examinations for Taste Over the Anterior Two Thirds of Tongue After Total Section of the Glossopharyngeal (IX) Nerve Intracranially

Patient	Age	Diagnosis	Operation	Time of Test	Results of Sensory Examination Over Trigeminal (V) Area	Time of Taste Perception		Control Tests (Before Operation)		Remarks
						Affected Side	Normal Side	Affected Side	Normal Side	
M (Case 1)	45	Glossopharyngeal neuralgia	Section of ninth nerve	10 days after operation	Normal	Sugar Salt Acid Bitter	Instantly Instantly Instantly Instantly	Not tested	Not tested	Complete loss of taste over the posterior third of the tongue
M (Case 2)	56	Glossopharyngeal neuralgia	Section of ninth nerve	7 days after operation	Normal	Sugar Salt Acid Bitter	1 second 1 second 1 second 1 second	Not tested	Not tested	Complete loss of taste over the posterior third of the tongue
M (Case 3)	32	Glossopharyngeal neuralgia	Section of ninth nerve	8 days after operation	Normal	Sugar Salt Acid Bitter	3 seconds 7 seconds 10 seconds 4 seconds	10 seconds 12 seconds 5 seconds 5 seconds	10 seconds 10 seconds 7 seconds 5 seconds	Complete loss of taste over the posterior third of the tongue

TABLE 3 (Group III)—Results in Examinations for Taste Over the Anterior Two Thirds of the Tongue After Total Section, Intracranially, of Both the Glossopharyngeal (IX) and the Trigeminal (V) Nerves

Patient	Age	Diagnosis	Operation	Time of Test	Results of Sensory Examination Over Trigeminal (V) Area	Time of Taste Perception		Control Tests (Before Operation)		Remarks
						Affected Side	Normal Side	Affected Side	Normal Side	
M (Case 1)	69	Oarenuma of the face and throat	Section of ninth and fifth nerves intracranially	7 days after operation	Complete anesthesia for all forms of sensation over the trigeminal domain	Sugar Salt Acid Bitter	30 seconds 35 seconds 10 seconds 20 seconds	40 seconds 20 seconds 20 seconds 20 seconds	25 seconds 25 seconds 25 seconds 15 seconds	Complete loss of taste over the posterior third of the tongue

Section of the left fifth and ninth nerves intracranially and of the great auricular nerve superficially was performed on Feb 21, 1928

Before operation, the following results for taste were obtained by an associate

	Left (Affected Side), Seconds	Right, Seconds
Sugar	40	25
Salt	20	25
Acid	20	25
Bitter	20	15

Seven days after operation, the same associate obtained the following results for the anterior two thirds of the tongue on the affected side only

	Left (Affected Side), Seconds
Sugar	30
Salt	35
Acid	10
Bitter	20

There was total anesthesia for all forms of sensation over the affected trigeminal area

*Summary*—This single instance of pure experimental lesions of the fifth and ninth nerves combined merely adds emphasis to the results of the two foregoing groups, namely, that the intracranial portion of neither the trigeminal nor the glossopharyngeal nerve conducts taste sensations from the anterior two thirds of the tongue

#### GROUP IV PURE SEVENTH NERVE LESIONS (INTRACRANIAL)

CASE 1—A young woman, aged 25, of normal appearance, was referred with the diagnosis of an unlocalized tumor of the brain Eight months before admission, headaches began This was one month before her baby was born Staggering occurred from time to time and made her fearful of crossing the street Deafness began in the right ear and soon became total During the last months of pregnancy, she had three attacks of projectile vomiting associated with severe headache Two months after the birth of her baby, she consulted an ophthalmologist because of blurred vision, he found bilateral papilledema and advised her to consult a neurologist Shortly afterward a cerebellar exploration was made in another clinic, but nothing was found Five months later, symptoms having steadily progressed, she entered the Johns Hopkins Hospital

The following positive observations indicated a right cerebellopontile tumor (1) bilateral papilledema, (2) bulging, tight, bilateral cerebellar decompression, (3) deafness (total) in the right ear, (4) diminished sensation over the right trigeminal area, (5) slight right facial weakness of the peripheral type, (6) staggering gait, (7) a positive Romberg sign falling to the right, and (8) ataxia on the right side

In view of the negative cerebellar exploration at which the cerebellopontile angle had presumably been exposed an injection of air was made There was bilateral hydrocephalus establishing the diagnosis of a subtentorial tumor

On May 23, 1921, a right-sided cerebellopontile tumor was totally removed. The right facial nerve was necessarily sacrificed. A spinofacial anastomosis was refused.

Tests for taste were made on Dec 20, 1928, or seven and one-half years after removal of the tumor. There had been no preoperative gustatory examination. All forms of sensation were normal over the domains of the trigeminal and glossopharyngeal nerves on the affected side.

	Right (Affected Side), Seconds	Left Seconds
Sugar	0	5
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 2—A rather obese woman, aged 49, was referred by Dr. Hugh Morgan, of Nashville, Tenn., with the diagnosis of a cerebellopontile tumor. Twelve years before he consulted us, tinnitus began in the left ear, there was some associated dizziness. Six years before, deafness began in the left ear and steadily progressed. Three years before, unsteadiness of gait was first noticed. It was present only at times. There had been spells of unconsciousness with subsequent weakness of the lower limbs, but no convulsions. Headaches began in the suboccipital region four months before we saw him. There had also been left occipital pains and stiffness of the neck.

On neurologic examination, the patient showed the positive signs of a left cerebellopontile tumor, i. e., (1) complete deafness of the left ear, (2) a staggering gait, (3) a positive Romberg sign, falling backward and to the left, (4) ataxia on the left side, and (5) bilateral papilledema.

The diagnosis was a left cerebellopontile tumor.

On Nov. 3, 1923, the tumor was totally removed. The facial nerve was sacrificed. Spinofacial anastomosis gave excellent return of function.

Complete recovery followed. The patient was living and well on Aug. 1, 1929.

No tests for taste were made before operation. The sensation over the domain of the left (affected side) trigeminal and glossopharyngeal nerves was unimpaired.

In December, 1928, five years after the tumor had been removed, an examination for taste by one of us (W. E. D.) showed

	Left (Affected Side), Seconds	Right, Seconds
Sugar	0	5
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 3—A sparely nourished woman, aged 33, was referred by Dr. Louis Hamman, of Baltimore, with a diagnosis of tumor of the brain. Her symptoms began five years before we saw her with pain and stiffness in the back of the neck. These pains had grown worse and more frequent during the past two years, and they had been accompanied by dizziness and ringing in both ears. On three occasions she had lost consciousness. For about one year, she had had increasing dimness of vision and transient diplopia. There had also been violent vomiting every few days for the past six months. This was not associated with the intake of fluid but rather with a sudden change of position. For three months she had been unable to walk without support. For the past year, she had been

much more irritable, unreasonable and irresponsible. For several months, there had been urgency and hesitancy in urination. Deafness was first noticed in the right ear two years before she consulted us.

Neurologic examinations disclosed a characteristic right cerebellopontile tumor, as revealed by the following symptoms: (1) total deafness of the right ear, (2) bilateral papilledema, (3) a staggering gait, (4) a positive Romberg sign, (5) ataxia on the right side, and (6) suggestive hyperesthesia over the right trigeminal area.

**Operation.** A right-sided cerebellopontile tumor was completely removed on Aug 5, 1927. The facial nerve was sacrificed, this loss of function was repaired by a spinofacial anastomosis two weeks later.

A test for taste was made by one of us (W E D) at the time of discharge from the hospital, eighteen days after operation, with the following results:

	Right (Affected Side), Seconds	Left, Seconds
Sugar	0	10
Salt	0	15
Acid	0	7
Bitter	0	10

Sensation on the affected side of the face was unimpaired.

**CASE 4**—A well nourished woman, aged 29, was referred by Dr. John Barron, of York, S. C. She complained of staggering and drawing of her face. Five years before we saw her, deafness was first noticed in her left ear. About a year before, the deafness became more pronounced and other symptoms developed. About the same time, there were headaches, attacks of dizziness and staggering, particularly when turning. Six months before examination, her gait became unsteady, she became worried and irritable and had frequent attacks of crying. The headaches became more frequent and more severe, especially during the menstrual periods. The headaches at first were frontal, and later became general. Vision was blurred and the patient had frequent attacks of diplopia. Four months before we saw her, numbness developed in the left side of the face, and at the same time her face drew to the right side and she was unable to close her left eye.

The following positive signs were disclosed on neurologic examination: (1) bilateral papilledema, (2) deafness in the right ear, (3) paralysis of the left side of the face, (4) a staggering gait, (5) a positive Romberg sign with falling toward the left, (6) nystagmus, and (7) bilateral ankle clonus and bilateral Babinski reflex.

On Sept 13, 1927, a large left-sided cerebellopontile tumor was completely removed. The seventh nerve was sacrificed, two weeks later a spinofacial anastomosis was performed to correct the facial deformity.

Examination for taste made by one of us (W E D) at the time of discharge, seventeen days after operation, showed the following results:

	Left (Affected Side), Seconds	Right
Sugar	0	Instantly
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

Sensation on the affected side of the face was unimpaired.

CASE 5—The patient was a normal appearing woman, aged 42, referred by Dr N G Wilson, of Norfolk, Va, with a diagnosis of tumor of the brain. The patient dated the onset of her present trouble to five years before we saw her, when she noticed a clicking, buzzing noise in the right ear. A month or two later she suddenly became deaf in that ear. She had very few symptoms, however, until a year before examination, when a tonsillectomy was done, immediately afterward she noticed numbness and loss of sensation in the right side of the face and the side of the cheek. At the same time pains which she considered sciatica appeared in both legs from time to time. For the past six months she had had staggering gait, with falling to the right. She had had some headache which concentrated in the right mastoid region and which was much intensified by straining at the stool.

The following positive neurologic observations indicated a right cerebellopontile tumor: (1) bilateral papilledema, (2) deafness in the right ear, (3) absence of corneal reflex on the right side, some loss of sensation in the right trigeminal area, (4) a positive Romberg sign, falling to the right, (5) a staggering gait, and (6) a positive Babinski reflex.

On May 5, 1925, a right-sided cerebellopontile tumor was completely removed. The right facial nerve was sacrificed, a spinofacial anastomosis was performed three weeks later. The patient has been well to the time of writing, Aug 1, 1929.

Tests for taste were made on July 20, 1928, over three years after the tumor was removed. There had been no preoperative tests for taste. All forms of sensation over the domain of the trigeminal and glossopharyngeal nerves on the affected side were normal. The results of the tests for taste made by one of us (W E D) were as follows:

	Right (Affected Side), Seconds	Left, Seconds
Sugar	0	5
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 6—A slender woman, aged 35, was referred by Dr Sydney Miller, of Baltimore, with the diagnosis of a tumor of the brain. Illness began two years before we saw her, with severe headaches in the frontal region on both sides. The headaches were usually associated with vomiting, which sometimes was suggestive of the projectile type. They had rather diminished in severity and frequency, though they were still very disturbing. Spells of dizziness began soon after the headaches, this persisted and was more marked when the patient moved about or turned the head suddenly. Impairment of hearing in the right ear was noticed about the same time, this had gradually progressed. The patient had felt weak in the knees. Her feet had seemed heavy. She had had the sensation of staggering.

Neurologic examination indicated a typical right-sided cerebellopontile tumor, as revealed by the following signs: (1) deafness of the right ear, (2) bilateral papilledema, (3) staggering gait, (4) a positive Romberg sign, with falling to the right, (5) ataxia on the right side, (6) nystagmus, (7) less active corneal reflex, and (8) diminution in sensation over the trigeminal area.

A right-sided cerebellopontile tumor was completely removed on Dec 14, 1927. The seventh nerve was routinely sacrificed in the removal of the capsule. A spinofacial anastomosis was done two weeks later to correct this deformity.

A test for taste made by one of us (W E D) at the time of discharge, twenty-seven days after the operation, gave the following results

	Right (Affected Side), Seconds	Left, Seconds
Sugar	0	15
Salt	0	3
Acid	0	3
Bitter	0	5

Some diminution of all forms of sensation over the right trigeminal area remained

CASE 7—A well nourished man, aged 37, was referred by Dr R A King, of Pittsburgh, with the diagnosis of a tumor of the brain. The symptoms began three years before our observation, with severe pains in the vertex. At the same time dizziness began to occur several times a day. He would stagger like a drunken man during these attacks. About two years before we saw him, weakness of the facial muscles on the right side was noticed. One year before, transient attacks of blindness appeared, lasting from a few seconds to a minute. Deafness antedated all of the symptoms mentioned, it began four years before examination and became complete two and one-half years ago.

Neurologic examination showed all the signs of a right cerebellopontile tumor, as follows: (1) bilateral papilledema, (2) weakness of the right external rectus muscle, (3) nystagmus, (4) absence of the corneal reflex, (5) diminished sensation over that side of the face, (6) partial right facial paralysis, (7) complete deafness in the right ear, (8) a staggering gait, (9) a positive Romberg sign, and (10) ataxia on the right side.

Operation. On May 5, 1927, a large cerebellopontile tumor on the right side was completely removed. Two weeks later a spinofacial anastomosis was done because of the facial paralysis resulting from the sacrifice of the seventh nerve.

At the time of discharge there still persisted a loss of the corneal reflex on this side and diminution of sensation over the right trigeminal area, this was less pronounced than before operation.

The following results were obtained in a test for taste made by one of us (W E D) at the time of discharge, three weeks after operation.

	Right (Affected Side), Seconds	Left
Sugar	0	Instantly
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 8—A feeble, emaciated woman, aged 58, was referred by Dr A E Fink, of Newark, N J, with the diagnosis of a cerebellopontile tumor. Three years before, she had influenza, followed by otitis media on the left side. The hearing in the left ear had since been impaired. For a year she had been totally deaf in the left ear and for the past six months she had noticed an instability of balance with a tendency to fall to the left when the eyes were closed, she had, however, never fallen. In the left ear there had been a noise like an engine.

Neurologic examination showed the following positive observations: (1) complete deafness in the left ear, (2) slight facial weakness on the left side, (3) diminished corneal reflex and impaired sensation on the left side, (4) a positive



Romberg sign and staggering gait, (5) nystagmus, and (6) ataxia on the left side

On April 24, 1926, a left cerebellopontile tumor was completely removed. The left facial nerve was sacrificed in removing the tumor.

An examination for taste, made by one of us (W. E. D.) two and one-half years after the operation, gave the following results:

	Left (Affected Side), Seconds	Right
Sugar	0	Instantly
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

There was a slightly diminished acuity for heat, cold and sharp over the left trigeminal area. There was no loss of sensation over the glossopharyngeal domain.

CASE 9—A normal appearing woman, aged 28, entered the Johns Hopkins Hospital to be treated for a tumor of the brain. Her first symptoms began two years before with beginning deafness in the right ear. Six months before admission to the hospital she became totally deaf in this ear, and the hearing on the left side had begun to diminish. For the past six months she had had a staggering gait. Three months before examination this became so severe that she fell on several occasions, always to the right side. At the same time her speech became thick and slurred, and difficulty in swallowing developed. Recently her right arm and right leg had been useless. She had had severe general headaches with intensification in the supra-orbital region, and more on the right side.

Neurologic examination indicated a right cerebellopontile tumor, as revealed by the following signs: (1) bilateral papilledema, (2) deafness in the right ear, (3) some diminution in sensation in the left side of the face, (4) slight facial weakness on the right side, peripheral in type, (5) staggering gait, (6) a positive Romberg sign, falling backward and to the right, (7) nystagmus, (8) ataxia and adiadokokinesia, and (9) bilateral Babinski reflex and bilateral ankle clonus.

A right cerebellopontile tumor was completely removed on July 16, 1926. The facial nerve was sacrificed. Fourteen months later an examination for taste made by one of us (W. E. D.) showed:

	Right (Affected Side), Seconds	Left, Seconds
Sugar	0	3
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

Sensory examination of the fifth nerve showed slightly diminished acuity for pin prick. Sensation for heat and cold was normal and equal on the two sides. There was no evidence of disturbance of the glossopharyngeal nerve.

*Summary*—This group offers the positive side of the taste problem. In every instance all forms of taste were immediately and permanently abolished when the facial nerve was divided intracranially. Taste therefore is conveyed to the brain stem from the geniculate ganglion by the intracranial portion of the facial nerve (the nerve of Wrisberg). So far as is known, these are the only pure experimental lesions of the intracranial portion of the facial nerve.

In the last four cases of this group the lesions were not pure, for some impairment of trigeminal sensation persisted. This was due to stripping the tumor from the sensory root of the trigeminus. The results, however, were identical with those for the pure lesions of the nerve as represented by the first five cases of the group.

#### GROUP V PURE SEVENTH NERVE LESIONS (PERIPHERAL)

CASE 1—A young girl, aged 17, was operated on for mastoid at another clinic eighteen months before we saw her. Since the operation there had been complete facial paralysis on the corresponding side. No other cranial nerves were affected. Sensation over the trigeminal and glossopharyngeal areas was normal.

A test for taste, made by one of us (W. E. D.) eighteen months after section of the facial nerve, gave the following results:

	Right (Affected Side), Seconds	Left
Sugar	0	Instantly
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 2—A well nourished man, aged 24, was operated on for chronic mastoid infection at another hospital ten months before we saw him. Since the operation the facial nerve has been totally paralyzed. There has been no loss of function in the trigeminal or glossopharyngeal areas. Hearing is still intact.

An examination for taste made by one of us (W. E. D.) gave the following results:

	Left (Affected Side), Seconds	Right
Sugar	0	Instantly
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 3—In a woman, aged 30, ten days before she came under our observation there was sudden complete paralysis of the facial muscles on the left side during the night. There had been a prodrome of pain in the mastoid region for thirty-six hours before paralysis developed. No other cranial nerves were affected. Hearing was normal. The trigeminal and glossopharyngeal sensory domains were normal.

An examination for taste made by one of us (W. E. D.) ten days after the paralysis gave the following results:

	Left (Affected Side), Seconds	Right
Sugar	0	Instantly
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 4—A man, aged 54, had an injury to the head fifteen months before we saw him. He was unconscious for twelve hours after which consciousness gradually returned. There was no weakness of either arm or leg after the accident and no disturbance of speech. His hearing was normal in both ears. Sensation over

TABLE 4 (Group IV)—Results of Examinations for Taste Over the Anterior Two Thirds of the Tongue After Total Section of the Facial Nerve Intracranially (in Removal of Cerebellopontine Tumor), Sensation Over the Trigeminal Domain Was Subsequently Intact in Five Cases, and Somewhat Impaired in Four Cases

Patient	Age	Diagnosis	Operation	Time of Test	Results of Sensory Examination Over Trigeminal (V) Area	Time of Taste Perception		Control Tests (Before Operation)	
						Affected Side	Normal Side	Affected Side	Normal Side
F (Case 1)	25	Cerebello pontine tumor	Total removal of tumor	7½ years after extirpation of tumor	Normal	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
F (Case 2)	49	Cerebello pontine tumor	Total removal of tumor	5 years after extirpation of tumor	Normal	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
F (Case 3)	33	Cerebello pontine tumor	Total removal of tumor	13 days after extirpation of tumor	Normal	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
F (Case 4)	29	Cerebello pontine tumor	Total removal of tumor	17 days after extirpation of tumor	Normal	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
F (Case 5)	42	Cerebello pontine tumor	Total removal of tumor	3 years after extirpation of tumor	Normal	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
F (Case 6)	35	Cerebello pontine tumor	Total removal of tumor	27 days after extirpation of tumor	Some diminution of all forms of sensation	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
M (Case 7)	37	Cerebello pontine tumor	Total removal of tumor	21 days after extirpation of tumor	Some diminution of all forms of sensation	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
T (Case 8)	58	Cerebello pontine tumor	Total removal of tumor	2½ years after extirpation of tumor	Slightly diminished perception of heat cold and sharp	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested
F (Case 9)	28	Cerebello pontine tumor	Total removal of tumor	14 months after extirpation of tumor	Perception of sharp diminished sensation otherwise unaffected	Sugar Salt Acid Bitter	0 Instantly Instantly Instantly	Not tested	Not tested

the trigeminal and glossopharyngeal areas was normal. There had been complete paralysis of the left side of the face since the accident.

An examination for taste, made by one of us fifteen months after the accident, gave the following results:

	Left (Affected Side), Seconds	Right, Seconds
Sugar	0	20
Salt	0	0
Acid	0	5
Bitter	0	30

CASE 5—A young girl, aged 15, was operated on at another clinic for chronic mastoid infection of six years' duration. Following the operation, twelve months before we saw her, she had complete paralysis of the right side of the face. No other cranial nerves were affected.

A test for taste made by one of us (W E D) at this time gave the following results:

	Right (Affected Side), Seconds	Left
Sugar	0	Instantly
Salt	0	Instantly
Acid	0	Instantly
Bitter	0	Instantly

CASE 6—A youth, aged 18, was operated on at another clinic for a chronic mastoid infection of ten years' duration. The operation was performed seven months before the patient came under our observation.

Tests for taste made by one of us (W E D) at this time gave the following results:

	Right (Affected Side), Seconds	Left, Seconds
Sugar	0	5
Salt	0	20
Acid	0	3
Bitter	0	7

CASE 7—A youth, aged 16, was operated on at another clinic for chronic mastoid infection of two years' duration. An operation was performed three months before we saw the patient.

A test for taste made by one of us (W E D) at that time gave the following results:

	Right (Affected Side), Seconds	Left
Sugar	0	Instantly
Salt	0	5 seconds
Acid	0	Instantly
Bitter	0	Instantly

CASE 8—A large, robust, well nourished man, aged 47, was referred by Dr F C Schreiber, of Washington, D C for treatment for Meniere's disease. One year before examination, when he awoke and raised his head to get out of bed he felt dizzy and vomited but had no nausea. For three days this dizziness

persisted and prevented him from getting out of bed. Every time he moved, the dizziness was intensified and frequently caused vomiting. After the third day he was able to get out of bed, but still remained more or less dizzy for three weeks, at which time the attack had entirely cleared. Four months later he had another attack, almost exactly similar to the previous one. This attack lasted one week. Six months after the first attack, partial deafness appeared in the left ear and, at the same time, tinnitus, both the deafness and the tinnitus came on suddenly during an attack of dizziness.

The neurologic examination showed partial deafness of the left ear, staggering gait and a positive Babinski reflex on the left side. The diagnosis was Meniere's disease.

On April 12, 1927, section of the eighth nerve, left, was performed. The facial nerve was accidentally injured, producing complete facial paralysis, for which a spinofacial anastomosis was done later.

The results of an examination for taste made by one of us (W. E. D.) after the operation were as follows:

	Left (Affected Side), Seconds	Right, Seconds
Sugar	0	0
Salt	0	5
Acid	0	5
Bitter	0	10

*Summary*—The results of these cases will clear any doubt which may yet remain that the facial nerve conducts sensations of taste from the point of union with the chorda tympani nerve with the geniculate ganglion. The results shown in group 4 indicate that the sensations of taste are conducted by the chorda tympani through the nervus intermedius, which represents the sensory portion of the seventh nerve of the gustatory nucleus in the pons.

#### SUMMARY OF RESULTS IN THE ENTIRE SERIES OF EXPERIMENTS

In this series of experiments on man, made after intracranial division of the different nerves presumably concerned with taste, several facts have been determined. Intracranial division at the brain stem of the glossopharyngeal nerve or of the sensory root of the fifth nerve or of both nerves is not accompanied by permanent loss of taste to the anterior two thirds of the tongue. Total loss of taste on the anterior two thirds of the tongue invariably follows intracranial division of the seventh nerve (at the pons) or of the peripheral portion at any point between its exit from the pons and the geniculate ganglion, from which point the fibers pursue a separate course.

At times there may be a temporary loss or diminution in acuity of taste following operations on the gasserian ganglion or the sensory root of the fifth nerve, but later taste returns to normal. Initial loss of taste, with subsequent return, has been noted by Koster and Cushing after operations on the gasserian ganglion. They assumed that another

[illegible]

Patient	Age	Injury	Operation	Post-operative condition	Result
F (Case 1)	17	Frontal paralysis	Mastoid	Complete recovery	Normal
M (Case 2)	24	Facial paralysis	Mastoid	Complete recovery	Normal
F (Case 3)	20	Partial paralysis	Mastoid	Complete recovery	Normal
M (Case 4)	31	Fractured skull	Mastoid	Complete recovery	Normal
F (Case 5)	19	Facial paralysis	Mastoid	Complete recovery	Normal
M (Case 6)	18	Facial paralysis	Mastoid	Complete recovery	Normal
M (Case 7)	16	Facial paralysis	Mastoid	Complete recovery	Normal
M (Case 8)	47	Meniere's disease	Section of auditory nerve	Two days after injury of facial nerve	Normal

nerve had taken over the function of conducting sensations of taste in these cases. It seems improbable in the present cases that another nerve will assume the function of conducting the sensation of taste. We have no experimental or clinical observations which will warrant such an assumption.

#### STUDIES ON A PATIENT WITH MULTIPLE, SMALL METASTATIC TUMORS OF THE CRANIAL NERVES

Despite the untrustworthiness of the gustatory changes produced by primary or secondary tumors involving nerves conducting sensations of taste, the case about to be recorded is different from those which have been reported. It is included in this paper only because the changes in taste were so closely and definitely associated with loss of function of the seventh nerve occurring first on one and then on the other side. At autopsy many tiny, discrete, secondary melanotic sarcomas were found in and along the nerves of the cauda equina, and a few nodules in the cranial nerves on both sides (fig 5).

Each nodule was so small that the tumor could cause only local destruction of the nerve involved, and could not press on adjacent cranial nerves. Moreover, the loss of taste occurred during the stay of the patient in the hospital and coincided exactly with the loss of function of the facial nerves.

A young man, aged 25, was under observation in the hospital over a period of three months. When first seen, his main complaint was referable to the cauda equina, but a peripheral facial paralysis was also noted on one side. In the early stages, the right facial paralysis was the only sign of intracranial disturbance. Taste was entirely lost over the anterior two thirds of the tongue on the right side. It was unaffected on the left side. Sensation, including the corneal reflex, was normal over the area of distribution of both fifth nerves. The action of the masseter, temporal and pterygoid muscles was unaffected. After a few weeks, paralysis of the left facial muscles began to develop. Within ten days this became complete, the typical mask appearance of bilateral facial paralysis developing. Coincidentally, taste was lost on the left side. Loss of taste was noted over the anterior two thirds of the tongue on both sides, though neither trigeminal nerve was as yet affected. Some time later, some involvement of the right trigeminus was noted. Although this gradually progressed, it never became complete. The left trigeminus was unaffected. Toward the end, the auditory, glossopharyngeal and vagus nerves were gradually affected. Total deafness finally ensued. Dysphagia was soon followed by total inability to swallow.

#### CONCLUSIONS

We find no evidence to support the theory that a variable nerve supply conducts the sensations of taste, as first advanced by Krause and more recently sponsored by Harris who accepted Nageotte's anatomic demonstration that the fifth, seventh and ninth nerves have a common gustatory nucleus in the pons.



Fig. 5—Drawing of brain showing numerous metastatic nodules in the cerebral nerves. The importance of this specimen in connection with the pathway of taste lies in the fact that the nodules destroyed both seventh nerves and both fifth nerves were unaffected except for a tiny nodule in the right motor root. Taste was lost on both sides (anterior two thirds of the tongue) while sensation over the sensory domain of the fifth nerves remained intact.



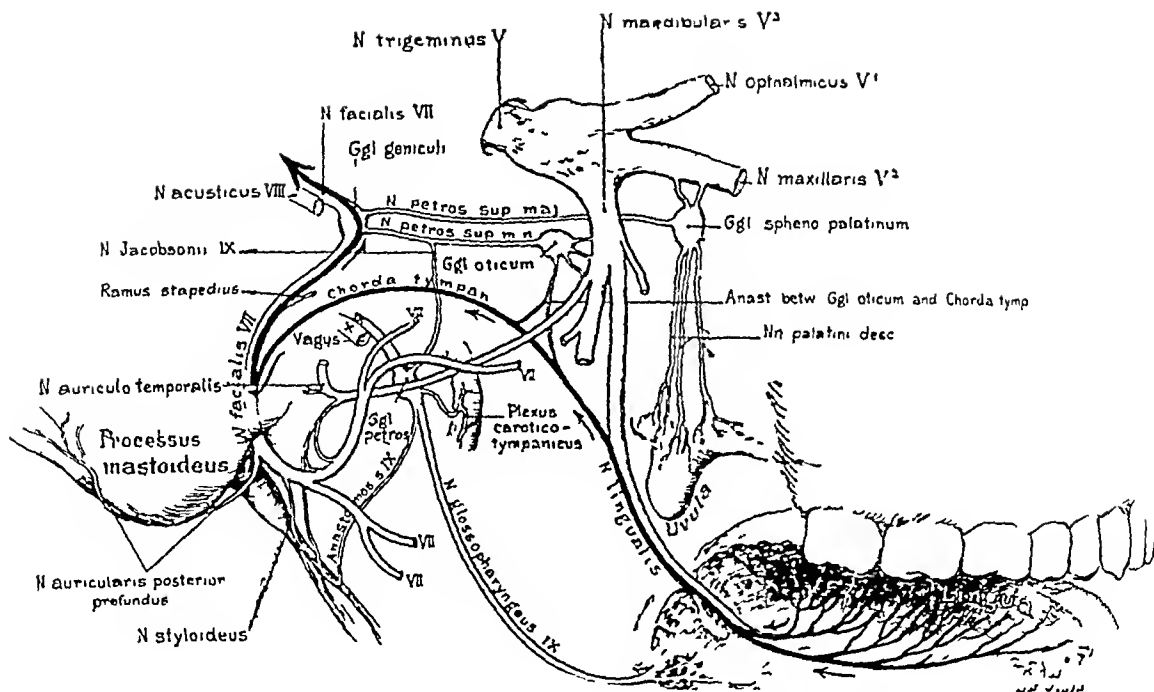


Fig 6—Pathway of taste from the anterior two thirds of the tongue as determined by our observations after intracranial division of the fifth and seventh nerves (Lewis and Dandy) This pathway was first suggested by Lussana

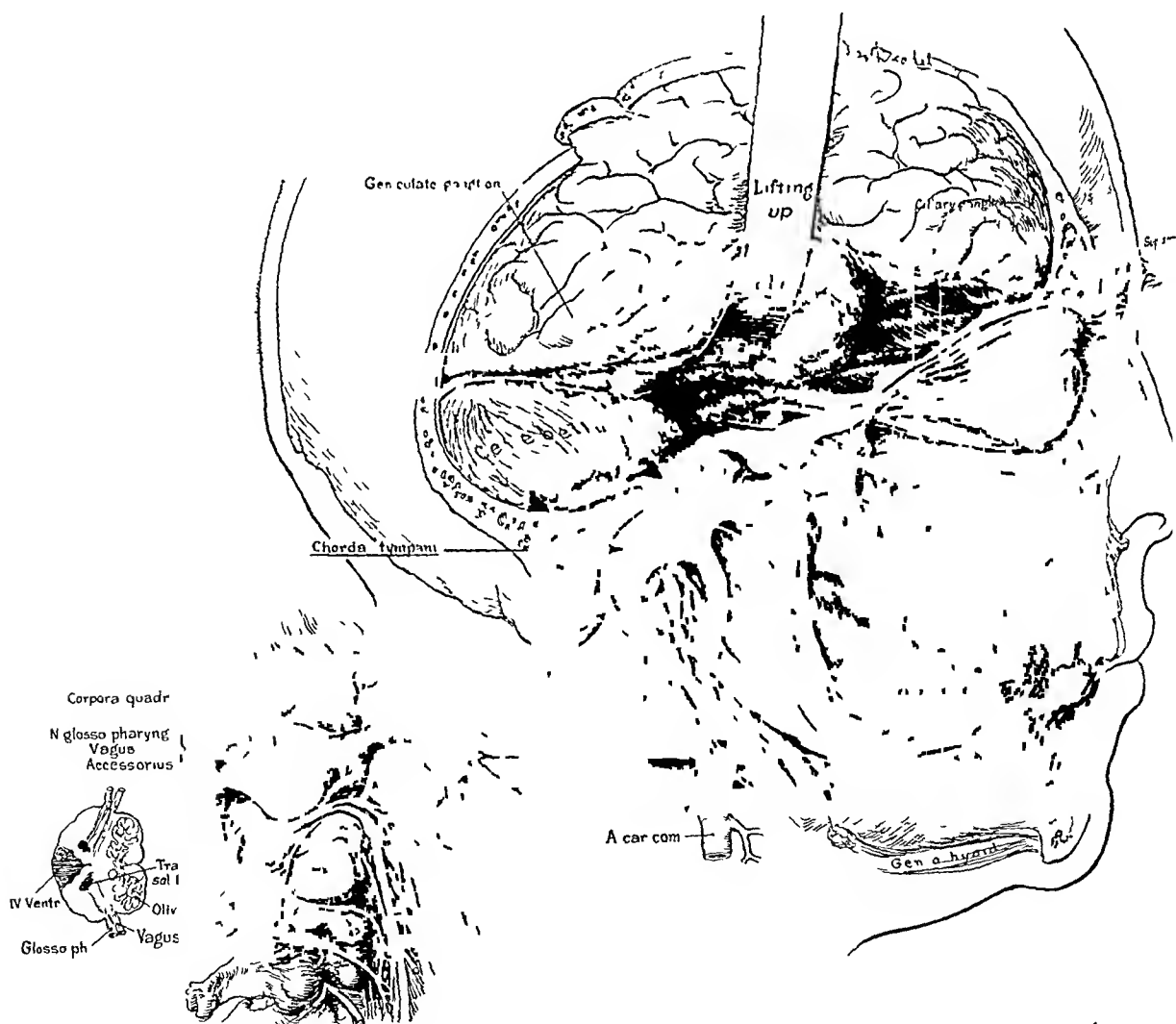


Fig 7—Drawing by Mr Brodel to show the course of the taste fibers which we believe to be from the tongue through the chorda tympani to the facial nerve thence directly through the geniculate ganglion and nerve of Wrisberg to the tractus solitarius in the pons

Our observations indicate that but one nerve conducts sensations of taste from the anterior two thirds of the tongue. This is the nervus intermedius (Wrisberg) or the glossopalatinus (Hardesty), which represents the sensory portion of the seventh nerve.

The course of the pathway of taste is direct. Stimuli pass from the taste buds through the chorda tympani by way of the geniculate ganglion and the nervus intermedius into the pons.

These conclusions are based on the results of intracranial division of the isolated cranial nerves in patients.

The following are the observations on which the conclusions are drawn: 1. Section of the sensory root of the fifth nerve is not followed by any permanent changes in taste, although in each instance all forms of sensation except taste over the trigeminal domain are totally absent. 2. After intracranial division of the seventh nerve, including the sensory portion (nervus intermedius of Wrisberg, the X glossopalatinus of Hardesty), taste to the anterior two thirds of the tongue is completely and permanently lost. 3. Division of the facial nerve, between the geniculate ganglion and the point at which the chorda tympani leaves the facial nerve to pass through the middle ear, is invariably followed by total and permanent loss of taste. 4. Intracranial division of the glossopharyngeal nerve is followed by complete and permanent loss of taste to the posterior one third of the tongue, but there is no effect on taste in the anterior two thirds of the tongue.

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# PAINFUL POSTOPERATIVE ABDOMINAL SCARS\*

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A considerable number of patients complain of postoperative soreness in the region of their scars, often of enough severity to interfere with the pursuance of their daily routine. Some of these conditions are often diagnosed as postoperative adhesions. Frequently, at secondary exploration, insufficient pathologic change is found to account for the symptomatology. A diagnosis of neurasthenia may be made as a result. It is my opinion that a certain number of these cases may be due to neuromas in the abdominal scar.

The literature in regard to neuromas or neuritis of the abdominal scars is scant, and it seems of sufficient import to review what literature there is and to report four cases which tend to show that this condition is more prevalent than is generally believed.

The microscopic proof of this lesion is extremely difficult, as the nerves traversing the scar tissue are extremely small and their identification in the excised tissue almost impossible.

The assumption that the symptoms and pathologic change in the four cases mentioned subsequently were due to neuroma or traumatic neuritis of the lower thoracic nerves is based on the following data:

- 1 In three cases the injection of procaine hydrochloride into the fascia of the right rectus muscle relieved the pain for various periods of time.
- 2 The patients in three cases were relieved from symptoms by excision of the scar tissue en bloc without opening the peritoneum. In the fourth case the peritoneum was opened to inspect the abdominal viscera, and there was insufficient pathologic change in the peritoneal cavity to account for the patient's symptoms.
- 3 The peripheral pain in amputation stumps has been definitely shown to be due to neuroma, and the microscope has confirmed this diagnosis.

As the process of repair, with contraction of scar tissue and injury to nerves, is similar in amputation stumps and in abdominal scars, it is reasonable to assume that postoperative pain in the abdominal wound may therefore be due to neuroma.

In order to refresh the memory an account of the anatomy of the lower six thoracic nerves is given (fig 1).

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\* Submitted for publication, Jan 29 1930.

\* Read at the Southern Surgical Association meeting Dec 12 1929.

## ANATOMY OF THE LOWER SIX THORACIC NERVES

The seventh, eighth, ninth, tenth and eleventh thoracic nerves differ from the upper thoracic nerves only in regard to a part of their course and distribution. Each has the same course and communications as the preceding nerves in the thoracic wall. In addition, these nerves have a further course and distribution in the abdominal wall. Each nerve traverses its intercostal space in the way described. At the anterior

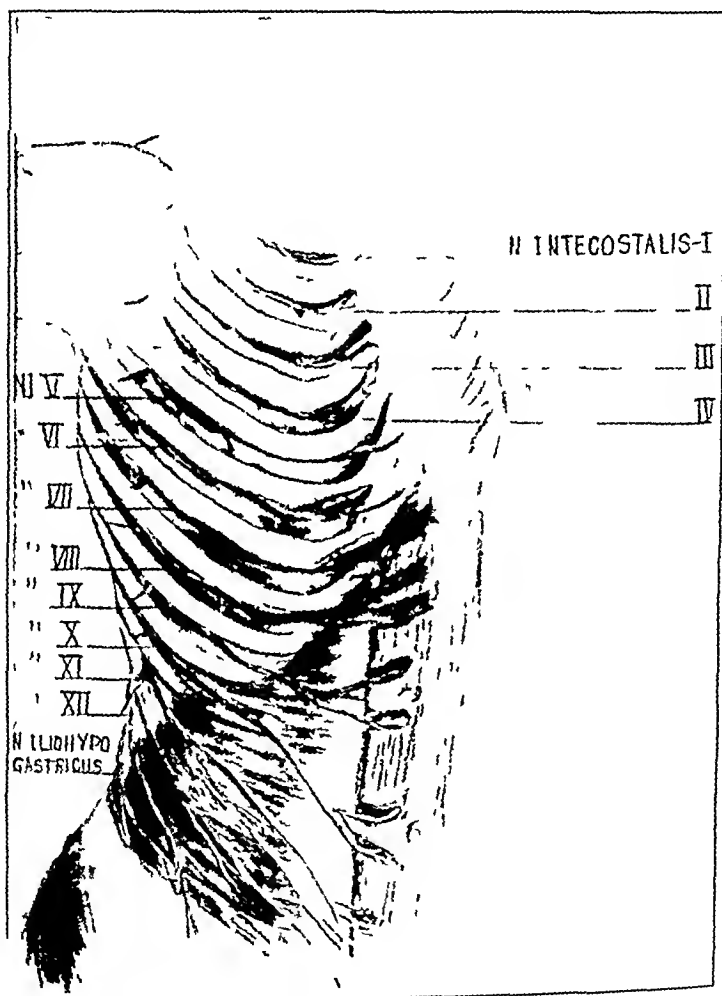


Fig 1—Diagrammatic sketch showing abdominal distribution of the lower six intercostal nerves. Note that the external oblique and the internal oblique muscles have been removed.

end of the space, the nerve pierces the attachment of the diaphragm and the transversalis abdominis muscles to the costal cartilages, and courses forward in the abdominal wall between the transversalis and obliquus internus muscles. The nerve then passes between the rectus muscle and the posterior layer of its sheath, and eventually reaches the anterior abdominal wall and becomes cutaneous by the piercing of the rectus itself and the anterior layer of its sheath.

*Muscular Branches* —The lower intercostal nerves supply the intercostal muscles of the spaces in which they lie, and in the abdominal wall they innervate the transversalis, obliqui and rectus abdominis. The branches arise from the main trunk as well as from the lateral and anterior branches.

*Cutaneous Branches* —The cutaneous branches are lateral and anterior. The lateral branches divide into anterior and posterior parts, and, becoming superficial along the line of interdigitation of the obliquus externus muscle with the serratus magnus and latissimus dorsi, they are directed more obliquely downward than the lateral branches of the higher intercostal nerves, and are distributed to the skin of the loin as low down as the buttock. The lateral branch of the eleventh nerve can be traced over the iliac crest.

The anterior branches are small. That of the seventh nerve innervates the skin at the level of the ensiform cartilage. The eighth and ninth appear between the ensiform cartilage and the umbilicus, the tenth nerve supplies the region of the umbilicus, and the eleventh the area immediately below the umbilicus.

The cutaneous branches of these nerves, including the posterior primary divisions, thus supply continuous belts of skin, which can be mapped out on the body from the vertebral column behind to the middle line in front. These nerves are not placed horizontally but tend to be drawn downward as the series is followed from the upper to the lower nerves.

The twelfth thoracic nerve is peculiar in its course and distribution. It emerges below the last rib and passes outward and downward in the posterior abdominal wall under cover of the psoas muscle, and between the external arcuate ligament and the quadratus lumborum muscle, it pierces the transversalis muscle, and courses forward in the interval between it and the obliquus internus as far as the sheath of the rectus muscle. After piercing the posterior layer of the sheath, the rectus muscle and the anterior layer of the sheath, it terminates by supplying the skin of the anterior abdominal wall midway between the umbilicus and the pubis. The branches of the nerve are the muscular, to the transversalis, obliqui, rectus and pyramidalis muscles of the abdominal wall, and the cutaneous, two in number—an anterior terminal branch, which supplies the skin of the anterior abdominal wall midway between the umbilicus and the pubis, and a large lateral cutaneous (iliac) branch, which, passing obliquely downward through the lateral muscles of the abdominal wall, becomes superficial above the iliac crest about 2 inches behind the anterior superior spine. It supplies the skin of the buttock as far down as a point below and in front of the great trochanter of the femur.



The twelfth thoracic nerve, in many cases, receives a communicating branch from the eleventh, near its origin, and still more frequently sends a fine branch to join the origin of the first lumbar nerve in the psoas muscle. It may communicate also with the iliohypogastric nerve, as they lie together in the abdominal wall.

When a nerve is cut completely or in part, the neuraxes start to grow in a straight line, if their growth is not interrupted. At the same time, however, there is a contraction of the scar tissue in the periphery of the scar, so that frequently thwarted neuraxes try to force their way through the scar tissue and twist themselves into spirals and corkscrew-like bodies. They are called perineuritic fibrils.

Jager and Traum studied this process of nerve regeneration in man in about fifty operative scars, mostly laparotomy scars, using more than 1,000 histologic sections. The process of nerve regeneration, as found in these studies, was as follows:

Degeneration resulted often from section of the nerve fibers at operation, and degenerative changes are evident in the nerve fibers in the first few weeks post operative. In a four weeks old scar, however, the products of nerve degeneration had disappeared. Nerve elements in a scar of this age were not demonstrable in the stratum papillare or reticulare as a rule, but in the tela subcutanea there were thin nerve fibers, usually grouped in bundles, extending to the epithelium. Other fibers followed the course of the arterioles and capillaries in the scar tissue. In older scars the nerve fibers advanced into the epithelium, and in scars ten or twelve weeks old had reached the stratum papillare. As they advanced the fibers tended more and more to show dichotomous division with the formation of collateral processes, which often anastomosed with neighboring fibers. Most of the nerve fibers in the scar tissue showed no medullary substance. No tendency to form encapsulated end corpuscles was observed in scar tissue. The nerve endings were primitive in type.

These authors, however, did not study the nerve repair in the deeper layers of the scar.

Quain and Eggers, in a review of painful scars observed during a routine examination of recruits for the army, found that pain in and about an abdominal scar, often deep seated or radiating to the back, was observed in a certain percentage of cases in a military hospital. They described several types of cases in which operations revealed either hernia or adhesions beneath the wound. They also stated that there is another type of painful scar which they were not able to demonstrate clearly in this series of cases—cases in which nerve fibers are caught in the scar and produce pain. To prove this condition, a local anesthesia can be injected into the abdominal zone containing the nerves leading to a scar and in the positive cases all pain will cease. Excision of the scar will bring about a cure.

In 1924, Marshall Clinton read a paper before the Section on Surgery of the American Medical Association, entitled "Subcostal

Neuritis as a Cause of Abdominal Pain" Clinton claimed that the lower intercostal nerves, particularly the eleventh and twelfth, as they pass beyond the tips of the last few ribs, are frequently susceptible to trauma. He claimed that the commonest cause of injury of the eleventh and twelfth nerves is by repeated squeezing of the nerve between the tips of the rib and the wing of the pelvis. This particular trauma is found in short-waisted persons or in those who have an unusually long eleventh or twelfth rib. The pain is characterized by being of a tooth-ache type, accentuated in the morning when the patient arises and bends over. The pressure under the tip of the eleventh or twelfth rib will reproduce this pain. The pain may also be produced by setting the patient in a chair and bending him to one side, then forward, and to the other side, which will start the pain as soon as the rib impinges on the edge of the wing of the pelvis. The relief, Clinton stated, is simple and immediate. The end of the offending rib should be dissected for 1 inch, and with it the underlying nerve trunk. Gross specimens show a neuroma-like swelling in the nerve trunk at the point of injury.

Corbett reported three clinical cases in which the condition was diagnosed by him as neuroma in postoperative cases. In the first case the patient suffered almost as much pain after nephrectomy for multiple stones as before. Neurologic examination showed a disturbance of sensation along the course of the ilio-inguinal nerve. A second operation revealed the fact that the nerve had been ligated, with the accompanying artery, and at the point of ligation a lateral neuroma had formed. Cutting the nerve completely relieved the patient's pain. In the second case there was pain in the distribution of the eighth dorsal nerve following resection of the rib and drainage for empyema. At a second operation a neuroma of the eighth nerve was found, which had apparently been caused by the sharp end of the cut rib impinging on the intercostal nerve. The third case was that of a patient with pain in the scar after an operation for benign tumor of the breast.

Corbett stated that in making a diagnosis of neuroma, the following points should be kept in mind. The pain in amputation stumps is referred to some part or parts of the missing limb, and in abdominal cases it is apt to be referred to the distribution of the involved nerve. If section of the nerve is complete the area of cutaneous distribution will exhibit anesthesia. If the division is partial, hyperesthesia and hyperalgia occur in about the same place. The neuroma itself is tender on pressure. Palpation sends sharp shocks of pain along the course of the nerve, and occasionally the neuroma may be felt. He stated that neurologic examination may reveal lesions of the nerve in patients presenting themselves for reoperation for adhesions.

I am unable to find any satisfactory reference in the foreign literature in relation to this condition.

The following four cases are reported, as I believe that if this condition is brought to the attention of surgeons, many more cases will be detected

#### REPORT OF CASES

CASE 1—S L, aged 30, a nurse, was operated on Oct 26, 1920, for chronic appendicitis. A right rectus incision was made. On the third day following operation she had so much pain in the abdominal wound that one of the clips was removed. As soon as she was up and about, she began suffering pain to the median side of the scar. This pain was steady, but became much worse when she became tired or nervous. The pain was so severe that in 1923 she reentered the hospital for observation. During this time she had some pain and rigidity in the region of the scar, associated with occasional vomiting. She lost 15 pounds (6.8 Kg) in weight. While in the hospital her condition was thoroughly studied, and roentgenograms of the gallbladder and gastro-intestinal tract were made, as well as gastric analysis and one duodenal pocket. It was thought that she might have some disturbance of the gallbladder. After leaving the hospital she was able to be up and about, but the pain still persisted—so much so that she took about 30 grains (1.87 Gm) of acetysalicylic acid and from 10 to 15 grains (0.65 to 0.97 Gm) of soluble barbital, U S P, or some similar preparation a day, in order to be able to keep on in her work. She had a second severe attack in April, 1925. At that time she had some nausea and vomiting, and tenderness in the region of the scar, with some spasm of the rectus muscle. At this time an exploratory laparotomy was done, through a median incision. There were no adhesions beneath the scar. One small omental band went to the appendix stump. This omental band was freed. The tubes and ovaries and the rest of the viscera were normal on palpation and inspection. When the patient left the hospital, however, the pain still persisted, and she was unable to return to work. In November, 1925, seven months after the exploratory laparotomy, I decided that she must have a neuroma, on account of the marked tenderness localized at the mesial side of the scar. It was decided to inject procaine hydrochloride to determine whether the pain would be relieved thereby. No relief was felt on injection of procaine hydrochloride into the skin or subcutaneous fat, but on injection into the deep fascia, almost immediate relief from pain was noted. This relief persisted for about three days, when the pain gradually recurred. Therefore in November, 1925, the patient was sent to the New York Hospital, and a resection of the abdominal wound, fat and fascia en bloc, down to the peritoneum, was performed. Care was taken not to ligate any nerve that might accompany a blood vessel. A specimen was sent to the laboratory to determine whether neuroma was present, but unfortunately it was left to dry, and hence no satisfactory examination could be made. The convalescence was uneventful. Since that time the patient has had no recurrence of the former pain, and has been able to do severe nervous and physical work without losing a day. She has had none of the former nausea, vomiting or abdominal pain.

CASE 2—R C, aged 31, was admitted to the Fifth Avenue Hospital on Feb 20, 1928, complaining of colicky pain in the right upper quadrant. She had had no nausea or vomiting. Eight years previously she had had an appendectomy through a right rectus incision. The pain was in the region of the scar and was exaggerated by the intake of food and by cathartics, and relieved at times by rest. The patient had had some symptoms suggesting hydronephrosis, and pyelograms showed a moderate dilatation of the pelvis of the right kidney. There was no definite evidence of stricture. On examination a well healed

abdominal scar was felt, with no evidence of hernia. There was definite tenderness on pressure to the mesial side of the scar at the upper angle. As the tenderness was so constantly marked in the region of the scar, and as the onset had occurred about one year following the previous operation, it was thought advisable to inject procaine hydrochloride into the fascia at the wound. One-half per cent procaine hydrochloride was used. After injection, the pain was completely relieved for two days. Operation was performed on February 29. An elliptical incision with scar tissue down to the peritoneum was made. A dermal suture was placed over the upper angle of the excised scar for identification in the laboratory. After excision of the scar, the peritoneum was opened and the abdominal cavity inspected. There was some adhesion of the omentum to the old scar. The gallbladder was palpated. It was thin and emptied easily. The kidney was palpated and seemed to be about normal in size, and no thickening could be felt in the region of the pelvis. The kidney could be moved only about 1 inch in a vertical direction. The uterus and ovaries were normal. The abdominal wound was then carefully closed in layers, care being taken to avoid clamping any nerves in the mass.

The pathologic report by E. S. Jessup was as follows: Section of the scar at the point indicated showed dense fibrous tissue and congestion of the vessels. No nerve tissue could be recognized, except a few small bundles near some blood vessels.

On June 10, 1928, the patient reported that the pain in the right lower quadrant had disappeared since operation, and that she could work without any handicap. She had lost the pain over the right hip, had gained 10 pounds (4.5 Kg.) in weight and was not constipated. She had no complaints.

On July 9, 1929, however, the patient complained of pain in the scar and a return of the original symptoms, which had become more marked. She stated that the pain was located in the upper angle of the incision, was tender on pressure and was made worse by coughing. Examination of the scar showed a large keloid, which was tender on pressure at the upper angle.

*Comment*—This patient had been treated for a hydronephrosis on the right side due to the pain in the back, while a pyelogram showed only a slight deformity. While the patient was in the hospital, the differential diagnosis between ureteral stricture and neuroma was discussed by the urologic and surgical departments. At the first follow-up, six months after operation, the patient's condition was satisfactory, and she was free from pain. A year later, however, she returned to the follow-up clinic with a keloid formation in the upper angle of the scar and pain in that region. As the eleventh thoracic nerve supplies the region of the incision, reflex nerve stimuli from a neuroma might easily be accountable for the pain she suffered in her back. The return of her symptoms following a keloid formation would seem to indicate that superficial fibulae coming from this nerve had again become caught in this scar.

CASE 3—B. W., admitted to the Lincoln Hospital on April 14, 1927, had been operated on for appendicitis in May, 1925. She complained of pain in the incision not accompanied by nausea, there was no constipation. The pain came on suddenly, especially on exercise, such as walking up stairs.

On physical examination there was tenderness superficially, which did not seem to be interabdominal. The provisional diagnosis was neuroma. On April 18, procaine hydrochloride was injected about the scar. On the following day, the patient stated that the tenderness which she had complained of on admission had almost entirely disappeared. A gastro-intestinal series showed the stomach to be normal in size and shape and to be situated low in the abdominal cavity. The duodenal cap was normal. There were no filling defects or other abnormalities. Examination after six hours showed the stomach to be empty and the head of the barium sulphate column just entering the cecum. An examination after twenty-four hours showed that the transverse colon was situated low in the abdominal cavity, but no other abnormality was noted.

Excision of the abdominal scar was made on April 22, 1927. An elliptical incision was made excising en masse the firm scar down through the interior of the rectus muscle to the peritoneum. The aponeurosis was then united with interrupted chromic and the skin with silk sutures, care being taken not to ligate any nerve accompanying a blood vessel.

The pathologic report was as follows. Section consisted of connective tissue, several thrombotic blood vessels and many fat cells. No nerve tissue was found.

The patient left the hospital free from pain, with a perfectly healed scar. Unfortunately, there was no follow-up in this case.

CASE 4—F A, aged 16, was admitted to the Fifth Avenue Hospital in May, 1929, complaining of pain in the right lower quadrant. She had been operated on in this hospital sixteen months before for chronic appendicitis, and had made an uneventful recovery. About three months after discharge she began to have pain, mostly in the region of the scar. This was accentuated when she bent over, was more severe at times and was associated with vomiting. The bowels were constipated. The urine was normal. One per cent procaine hydrochloride was injected into the scar and rectus sheath, which relieved the pain entirely for one day.

The scar from the former incision was excised with fusiform incision. This was carried down to the fascia of the external oblique muscle, which was carefully dissected to expose the scar. The small scar in the external oblique was not over the region lateral to the rectus sheath, but was at the margin. A small opening had been made accidentally in the anterior layer of the rectus sheath, and through this the region under the appendix scar was examined. It did not show anything to warrant further exploration in the rectus sheath. The aponeurosis of the external oblique was split in the direction of the fibers inward and outward. The only evidence of the deformed anatomic structures of the former operation was a little irregular fibrous band in the rectus sheath. The outer flap of the external aponeurosis was used to overlap the small defect made in the rectus sheath. The wound was closed with interrupted chromic sutures, the pocket and fat with interrupted plain sutures and the skin with skin clips.

On Oct. 20, 1929, the patient was entirely symptom-free and had been free from pain since the operation in May of that year. The excision of the painful scar had entirely relieved her from all the symptoms. The scar resulting from the second operation was ridged up and slightly wider than one would expect. The patient evidently developed keloid readily, otherwise her general condition was good. She was advised to use mercurial ointment on the scar every other night to determine whether this would have any effect.

## COMMENT

After a study of these cases, I am convinced that injuries to the nerve are more common in abdominal wounds than is generally recognized. Moreover one sees numerous cases of diminished tension of muscles when nerves have been cut. While one does not see evidence of definite hernia, one does see relaxed and atrophied muscles which must cause some functional interference. I believe that the methods of operative approach for the abdominal cavity must be reconsidered. The tendency has been to attempt to follow muscle planes, and frequently to sacrifice ruthlessly the accompanying nerves. It is known that muscles heal kindly, even if cross-cut, provided there is no infection. It would therefore seem that surgeons should readjust their ideas to attempt to place incisions so that they run parallel with nerves. If this theory is adopted, how is one to approach the abdominal cavity? The following suggestions are made.

I believe that, whenever possible, incision through the right rectus muscle should be eliminated from the surgeon's armamentarium. After several years spent in a follow-up clinic, I feel firmly confident that this incision is inadvisable for the following reasons: 1. Percentage of hernias after a right rectus incision is higher than after most incisions. 2. Frequently weak wounds are encountered, wherein the portion of the rectus muscle medial to the scar is paralyzed or at least inhibited in action. 3. Injuries to the nerve are more apt to occur when this type of incision is made. In making a right rectus incision one frequently encounters the deep epigastric vessel. There is usually a considerable amount of hemorrhage, and it is impossible to isolate the nerves going to the muscle, so that it is easy to place a ligature about both vessel and nerve. Frequently hematomas result from the injury to the vessel, and in some cases definite thrombosis has been noted along the course of the vessel, extending as far as the femoral vein.

In the upper right rectus incision the transversalis fascia runs directly from the intercostal margin to the mesial line as a well developed layer. It is difficult to close this layer by sutures. When the patient vomits or coughs, the spread of the ribs puts extreme tension on the suture line. Tearing of the fascia is frequently the forerunner of a ventral hernia.

If the surgeon prefers an incision to the right of the median line, either for exploration or for a better approach to the appendix, the Kammerer modification seems preferable to the usual right rectus incision. When the rectus muscle has been drawn to the mesial side, the nerves can be easily identified and retracted up and down, so as to allow a satisfactory exposure. Moreover, if it is necessary to sacrifice a nerve, it can be done under the eye, so that no unnecessary ligature is placed about it. In this type of incision, deep epigastric vessels are not encountered, and therefore there is less hemorrhage (fig. 2).

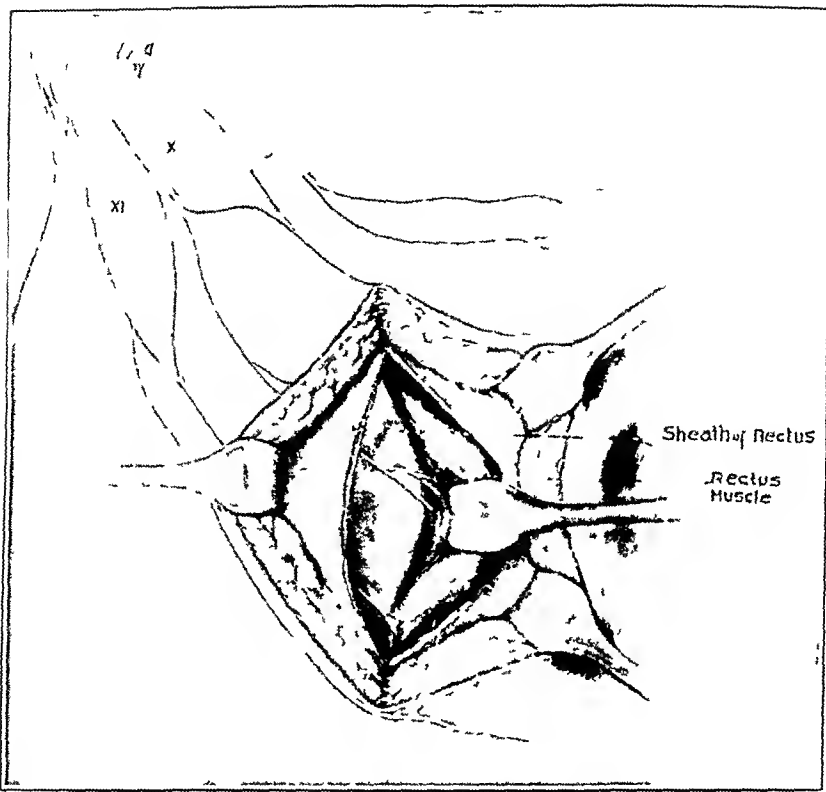


Fig 2—The Kammerer incision The rectus muscle is drawn mesially The nerves may be seen entering the rectus muscle and can be retracted either upward or downward If more exposure is needed, they may be cut without ligation

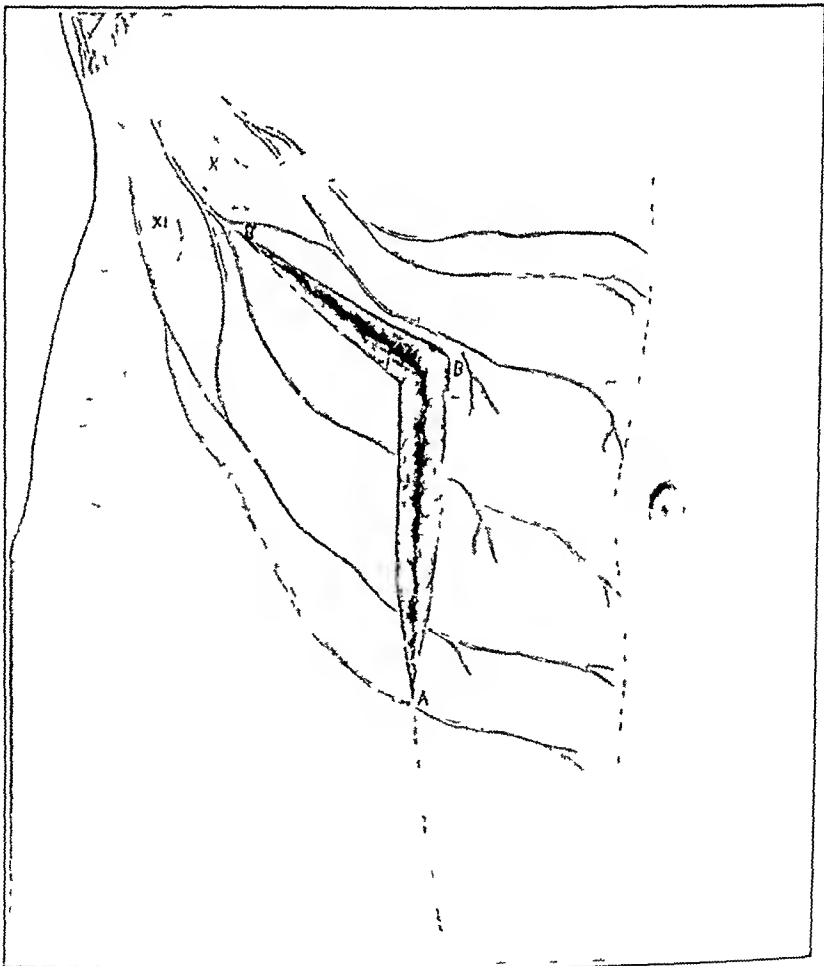


Fig 3—Extension of right rectus incision (Kammerer) for exposure of gallbladder B'-B extension is parallel to nerves so that only one nerve is cut during exposure

Often the surgeon wishes to remove an appendix, and at exploration finds pathologic changes in the region of the gallbladder. The problem then presents itself whether to enlarge the incision—with the possibility of a weak scar—or to close the lower incision and make a second one, with the resultant loss of time. I suggest that if a Kammerer incision has been made, the wound may be extended by a high oblique incision—one parallel to the McBurney incision—which begins at the rectus sheath and ends at the ninth costal cartilage in the mammary line. By this incision it is necessary usually to cut only one nerve, that at the upper angle of the Kammerer incision. This nerve can easily be seen at the first incision, and can be cut without danger of ligating it with the accompanying vessel. The extension of the incision runs parallel to the course of the intercostal nerves. A satisfactory exposure can be obtained thereby (fig. 3).

Upper or lower paramedian incisions are satisfactory, because neither vessels nor nerves of any considerable account are encountered.

The McBurney and the low Pfannensteil incision are ideally planned to avoid trauma to the nerves. The Kocher incision for exposure of the gallbladder involves the risk of injuring nerves, but less so than the right rectus incision.

Transverse abdominal incisions, extending either to or through the rectus muscles, are preferable to lateral vertical incisions, as fewer nerves are encountered and as cut muscles heal satisfactorily after suture.

#### CONCLUSIONS

1 Injuries to the nerves in abdominal incisions followed by neuromas or neuritis are more prevalent than is generally recognized.

2 They are probably often produced by ligating a blood vessel with its accompanying nerve.

3 In the cases reported in this article the right rectus incision was the procedure followed.

4 Diagnosis of neuroma may be made by testing out the sensory distribution of a nerve and by causing a cessation of the pain by temporarily blocking the nerve by injecting procaine hydrochloride. In right rectus incisions this is accomplished by injecting procaine hydrochloride beneath the fascia of the right rectus muscle.

5 Incisions for abdominal exposure should be planned to avoid trauma to the nerves. Mass ligation of vessels in the vicinity of nerves should be carefully avoided.



# THE EFFECT OF ACUTE EXPERIMENTAL CHOLECYSTITIS ON THE EMPTYING OF THE GALLBLADDER \*

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Mann,<sup>1</sup> in 1921, first reported the production of specific cholecystitis by the intravenous injection of Dakin's solution (a solution of chlorinated soda) At that time, however, studies were not made on the emptying time of such acutely inflamed gallbladders, as there was no evidence to show that the gallbladder emptied Many attempts were made to produce chemical cholecystitis by the use of a solution of chlorinated soda subsequent to the discovery that the gallbladder emptied after the ingestion of a meal of fat, but because of variation in the commercial product, positive results were not attained In the light of present, recently acquired knowledge concerning the emptying of the normal gallbladder following a fat meal, I was prompted to determine whether or not an acutely inflamed gallbladder empties, and to what extent such emptying occurs following the ingestion of a meal rich in fat

## METHOD OF STUDY

In these studies on the production of specific cholecystitis by chemical means, as well as the effect on the emptying of such diseased gallbladders, dogs were used Pathologic changes were produced within the wall of the gallbladder by the intravenous injection of varying amounts of eusol (a solution of boric acid) Animals were placed on a fast three to four days prior to operation, and explored four hours after the administration of a meal of egg yolk and cream Through a median line incision, direct observations were made on the degree of cholecystitis and the site of the lesions in the gallbladder, as well as on the emptying of the viscus The latter data were substantiated by additional observations which will be discussed more in detail under the heading "Operative Procedures" Finally the contents of the gallbladder were aspirated and an equivalent amount of iodized poppy seed oil, 40 per cent, was injected, care being taken not to soil the peritoneal cavity

## SOLUTION AND INJECTION

Animals in good general condition were selected, without any special reference to age, weight, size or sex Although previous observations on the production of specific cholecystitis by chemical means in which Dakin's solution was used had been made, there still remained certain

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\* Submitted for publication Sept 9, 1929

\* Work done in Division of Experimental Surgery and Pathology

1 Mann, F C The Production by Chemical Means of a Specific Cholecystitis, Ann Surg 73 54, 1921

disadvantages in connection with its use. A solution of eusol originally prepared by the Edinburgh unit during the World War seemed less toxic, the margin of safety seemed greater, thrombosis of the veins was seldom encountered and hemostasis was more easily controlled than when Dakin's solution was used. The solution for injection is prepared by placing 12.5 Gm. of sodium hypochlorite (chlorinated lime, Drackett) and 12.5 Gm. of crystalline boric acid in a large beaker in 1,000 cc. of distilled water. The solution is allowed to remain over night, is filtered once through filter paper the next morning and is ready for use after being warmed slightly to body temperature. All injections were made into the jugular vein. A definite dosage cannot be prescribed for each kilogram of body weight as an assurance of the development of inflammatory lesions within the wall of the gallbladder, and experiment has shown that an animal receiving 30 cc. for each kilogram of body

TABLE 1—*Varying Amounts of Eusol Injected for Production of Different Degrees of Cholecystitis*

Dog	Weight, Kg	Eusol, Cc	Cholecystitis, Grade	Eusol, Cc for each Kg of Body Weight
1	23.5	control	control	control
2	22.8	440 (in 2 injections)	1	15.2
3	20.0	400 (in 2 injections)	1	20.0
4	10.4	243 (in 2 injections)	2	23.3
5	12.3	200 (in 2 injections)	2	16.7
6	20.5	500 (in 2 injections)	3	24.4
7	6.0	250 (in 3 injections)	3	41.7
8	10.0	90 (in 1 injection)	4	9.0
9	10.5	135 (in 1 injection)	4	12.8
10	11.8	320 (in 2 injections)	4	27.1
Average	14.8	258 (in 2 injections)	1 to 4	19.0

weight in one or two injections would be certain to reveal definite pathologic changes in the wall of the gallbladder. However, such amounts are seldom necessary, and the risk is too great to chance invaliding the animal and thereby disturbing normal physiologic and metabolic processes. Experimental data in this direction seem to indicate that an average of about 20 cc. for each kilogram of body weight (table 1) would be a good index of the production of such lesions. Furthermore, the rapidity with which the solution is injected into the circulation is significant. Repeated observations have shown that eusol may be injected so slowly in very large quantities that changes in tissue are not produced, or so rapidly that the animal rapidly succumbs during the injection, with or without the production of any lesion of the gallbladder. Although it is not yet certain what the causative agents are in the production of such lesions of the gallbladder after the injection of eusol, it is believed that calcium plays a much more significant part than does chlorine or its associated compounds.

Positive results follow the injection of large amounts of eusol only after considerable experience in this direction. There is without question an individual susceptibility, not only to the toxicity of the solution, but in the production of lesions within the wall of the gallbladder as well. In one animal the lesions may develop after the administration of 40 cc., whereas in another animal of the same weight, sex, age and under the same conditions receiving 400 cc., lesions cannot be produced. Experimental data have shown that the condition of the gallbladder may be prognosticated with a high degree of certainty, not so much with reference to the degree or grade of cholecystitis, as to the presence or absence of lesions in that particular organ. Likewise, as experimental data have accumulated on this subject, it has been shown that a high percentage of inflamed gallbladders can be produced by this method. In the last ten animals injected by such measures, more than 80 per cent revealed lesions of the gallbladder, at least in some degree.

The specificity of Dakin's solution for the gallbladder has been referred to repeatedly in the literature, and undoubtedly the same is true of eusol, as it is a modification of Dakin's solution in which sodium carbonate is replaced by boric acid. Nevertheless, one finds, occasionally, lesions elsewhere in the body, which may be explained by the injection of unnecessarily large amounts of the solution in an attempt to produce a severely inflamed gallbladder. In this series of experiments, however, operation showed that all gross pathologic changes within the abdomen were confined to the gallbladder.

#### OPERATIVE PROCEDURES

The degree of cholecystitis at the time of exploration was estimated on the basis of grades 1 to 4. Cholecystitis graded 1 consisted of a few small hemorrhagic lesions anywhere in the wall of the gallbladder, cholecystitis graded 2 represented five or six such lesions, and cholecystitis graded 3 or 4 represented widespread hemorrhagic involvement of the entire wall of the gallbladder. It is clear from this classification that although there are only slight variations between grades 1 and 2 or between grades 3 and 4, there are decided differences between grades 1 and 4. Various degrees of cholecystitis are represented in this series, including two each of grades 1, 2 and 3, and three of grade 4, so that certain observations have been made possible. The series of ten animals was divided into three distinct groups, between which only slight variations in the procedure were maintained (table 2).

The three dogs in group 1 were given intravenously 0.05 Gm. of rose bengal for each kilogram of body weight in a 5 per cent solution in distilled water. The animals were then placed on a fast for from three to four days, during which time the dye was permitted to concentrate in the gallbladder. Through a median line incision four hours after the ingestion of a test meal, direct observations were made of the lesions, with notations on the emptying of the gallbladder. The latter data were corroborated by exploration of the duodenum directly above the entrance of the common bile duct and by noting any recent excretion of the dye on the duodenal mucosa. A sudden deposition of the rose bengal on the duodenal mucosa was easily recognized, and confirmed any contraction of the

gallbladder that might have taken place. It is reasonable to assume in this regard that four days were sufficient for the bile ducts to free themselves from any gross trace of the dye. The duodenum was closed in two layers by the Connell suture method. The content of the gallbladder was then aspirated, and an equal amount of iodized oil was injected. The abdomen was closed in four layers in the usual manner, and the animals were returned to the kennels to recover from the effects of the anesthetic. The fast was continued. From six to eight hours later, roentgenograms of the gallbladder were taken, after which a second meal of egg yolk and cream was given. Roentgenograms were then taken at frequent intervals so that any emptying of the gallbladder might be observed.

In group 2 (three dogs), the procedure was the same, except that the dye was omitted and the duodenum was not explored. Such a procedure would tend to eliminate any criticism that the motor activity of the duodenum and its nerve supply had been disturbed.

In group 3 were the remaining four dogs, including one dog which was used as a control. The animals were treated as were those of group 2, except that the mixture of egg yolk and cream was omitted previous to operation, and roent-

TABLE 2—*Observations in Three Groups of Animals Representative of Various Degrees of Cholecystitis*

Group	Dogs	Direct Observations				Roentgen Observations		
		Fat Meal, 4 hours Previous to Exploration	Rose Bengal	Duodenum Explored	Gallbladder Bile Aspirat- ed, Lipiodol Injected	Chole- cys- titis, Grade	Fat Meal, Hours After Exploration	Results
1	3	+	+	+	+	1, 2, 4	8	No emptying
2	3	+			+	1, 3, 4	8	No emptying
3	3 and control				+	2, 3, 4	24	Slight emptying in a case of cholecystitis, graded 4

genograms of the gallbladder were not taken until twenty-four hours after exploration. The slight variations within the last group would remove the possibility of any fatigue of the emptying mechanism of the gallbladder.

In most instances, the animals prior to operation lapped their meal of egg yolk and cream vigorously and appeared like normal healthy animals. If vomiting occurred that could not be controlled the animal was omitted from the study. Occasionally, a dog had to be encouraged to swallow the egg yolk and cream. This was accomplished either by inserting the tip of a syringe into the buccal fold or by slowly administering the contents by means of a small beaker. The stomach tube was never resorted to for fear of its inhibitory action on the mechanism of the gallbladder.

In every case following the administration of egg yolk and cream previous to operation, the absorption of fat was found to be good and the lymphatic channels, as well as the mesenteric lymph nodes as far down as the ileum, were well engorged. This seems to indicate that the mechanism of absorbing fat had not been disturbed to any decided degree.

Such direct observations did not disclose evidence to indicate that contraction of the inflamed gallbladders might have taken place follow-

ing the administration of the usual fat meal. Exploration of the duodenum in group 1 has substantiated the observations, as rose bengal was never seen on the duodenal mucosa. The observations seem to indicate that contraction of the acutely inflamed gallbladder does not take place following the usual test meal.

An observation made at operation included the rather marked distention of the gallbladder in all animals with cholecystitis graded 1 to 3 inclusive. It is estimated that the gallbladder was increased from a fourth to a third of its normal size. These observations seem to substantiate those of Bollman, Mann and DePage<sup>2</sup> made in 1925, in which they demonstrated that the concentrating function of the gallbladder may be impaired or totally lost in the presence of an acute inflammatory process. However, if cholecystitis was graded 4, the gallbladder was always found to be decreased in size from what would be expected from the size of the animal. Nevertheless, on aspiration the bile did not appear to be thickened or as concentrated as in the normal animal. Also, the biliary tract was found to be dilated in cases of advanced pathologic changes, although changes could not be detected about the cystic or common bile ducts. That the ducts were patent has been confirmed repeatedly both at operation and at necropsy, by pressure on the gallbladder, as well as by histologic examination. Even in the absence of serial sections, it is believed that obstruction to these passages was not present. It may be noted that in not a single instance has jaundice been observed following the production of cholecystitis, even though animals have been observed as long as three weeks after the injection. Therefore, it seems that the cystic and common bile ducts play little, if any, part in this pathologic entity, for at no time did the hemorrhagic exudate extend to that particular region. In some of the more advanced grades of acute cholecystitis, the gallbladders were reduced in size from a sixth to a fourth the capacity of the normal gallbladder. Bile could enter the cystic duct without difficulty, for in some instances of the more advanced grades of chemical cholecystitis, rose bengal was not administered until after the inflammation had been produced, and then there was no apparent difficulty in recovering the dye in high concentration from the lumen of the gallbladder. From examination of gross as well as microscopic sections of such gallbladders, it is difficult to understand how concentration of the bile could occur following such severe inflammation of the wall of the gallbladder. The size and appearance of the gallbladders in cholecystitis graded 4 may be explained, therefore, by the inability of the wall to expand.

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2 Bollman, J. L., Mann, F. C., and DePage, P. The Effect of Specific Cholecystitis on the Bile Concentrating Activity of the Gallbladder, *J. Lab. & Clin. Med.* **10** 544, 1925.

further because of the severe inflammation rather than by any other peculiarities incidental to the condition

#### PATHOLOGIC CHANGES AND COMPLICATIONS

The pathologic changes following the injection of eusol are not much different from those described by Mann following the injection of Dakin's solution. Lesions of the gallbladder appear as small, sub-peritoneal hemorrhagic areas resulting from marked breaking of the capillaries and infiltration of the wall. They vary in size from 1 to 20 mm and are situated anywhere over the area of the gallbladder. The wall appears to be thickened, indurated and more or less edematous,

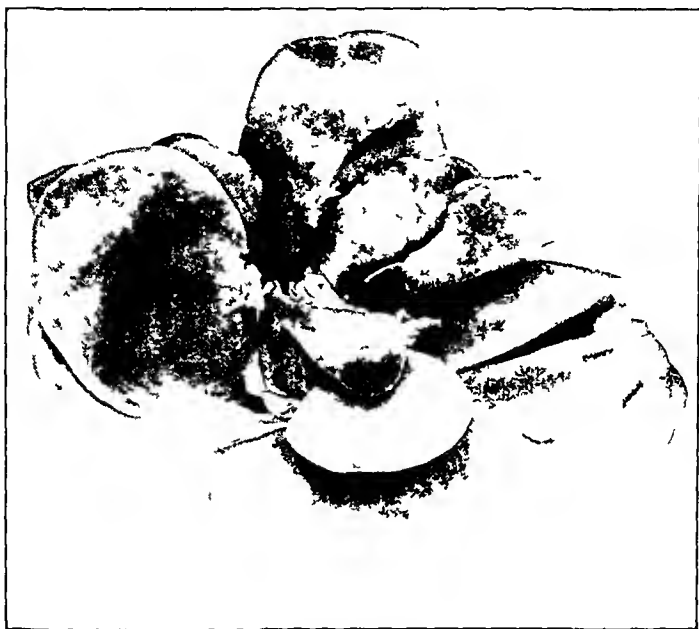


Fig 1—Large areas of a hemorrhagic exudate with marked induration, edema and increased thickening of the wall of the gallbladder. A hematoma may be noted at the fundus of the gallbladder.

with a generalized deep purplish discoloration besides the hemorrhagic areas (fig 1). The superficial vessels coursing about the viscus are always found to be dilated with frequent small areas of a hemorrhagic exudate along their route where the vessel has ruptured. A microscopic examination confirms the gross observations by revealing large areas of hemorrhage. In the less advanced cases of cholecystitis, the hemorrhagic exudate is usually confined to two distinct layers—the sub-epithelial layer between the mucosa and muscularis, and the perimuscular layer (figs 2 and 3). In such instances the areas are frequently so large and well circumscribed as to appear like a large blood vessel. The connective tissue and muscle fibers are well spread apart, giving

the appearance of marked infiltrating edema. In the more advanced cases, the exudate does not appear to be limited and is spread throughout the entire thickness of the wall extending from the subepithelial to the subserosal areas. The mucosa has seldom, if ever, been found to be affected (fig 4). The wall of the gallbladder is always decidedly thickened, the extent of thickening depending on the degree of involvement. In only one instance, in which many observations were made, has hemorrhage ever been encountered within the lumen of the gall-



Fig 2—A section through the wall of the gallbladder in mild cholecystitis. The hemorrhagic exudate is confined to two distinct layers,  $\times 150$

bladder. In a few cases, small hematomas about 1.5 cm in diameter were found within the wall. The liver appeared to be of the fasting type, with a moderate degree of fatty infiltration. On microscopic examination, marked congestion was found. The sinusoidal areas were engorged and distended with erythrocytes, and the cellular infiltration within the columns of cells was only slight.

Occasionally, in certain cases, numerous minute subperitoneal petechial hemorrhages were found at the base of the mesentery involving the entire gastro-intestinal tract. This may occur even in the

absence of a lesion of the gallbladder. Marked reactions of the gallbladder were noted fifteen minutes after the injection of the solution into the blood stream.

The most common complication that may develop after the use of eusol, aside from acute toxemia, is edema of the lungs. The lungs

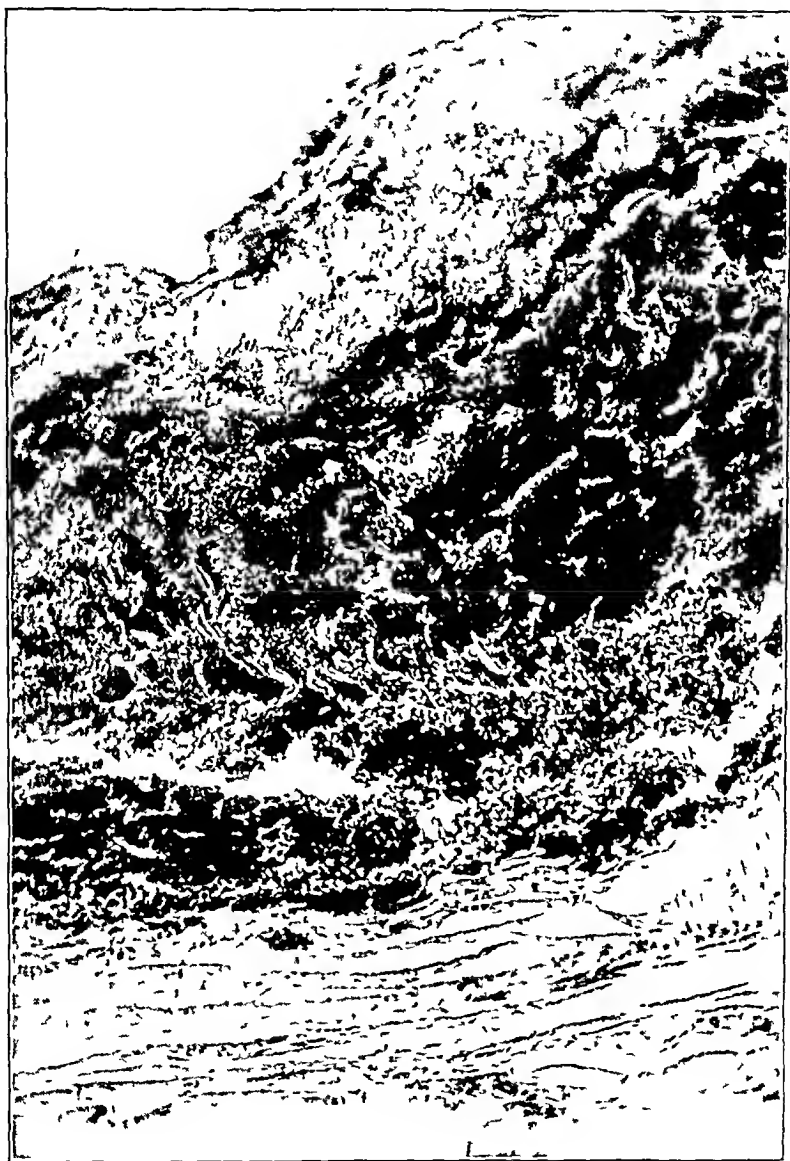


Fig. 3—A section through the wall of the gallbladder in severe cholecystitis; hemorrhagic exudate extends from the mucosal to the serosal areas,  $\times 150$

become water-logged and large amounts of frothy material are easily expressed. In two instances marked intra-abdominal hemorrhage was found, which resulted from rupture of the large mesenteric vessels. However, hemorrhagic nephritis and hemorrhagic gastro-enteritis so



frequently encountered after the injection of Dakin's solution have never been observed following the injection of eusol. Although there is little question that eusol is the more ideal as compared to Dakin's solu-



Fig 4—A section through the wall of the gallbladder in moderate cholecystitis. Absence of any involvement of the mucosa may be noted,  $\times 500$

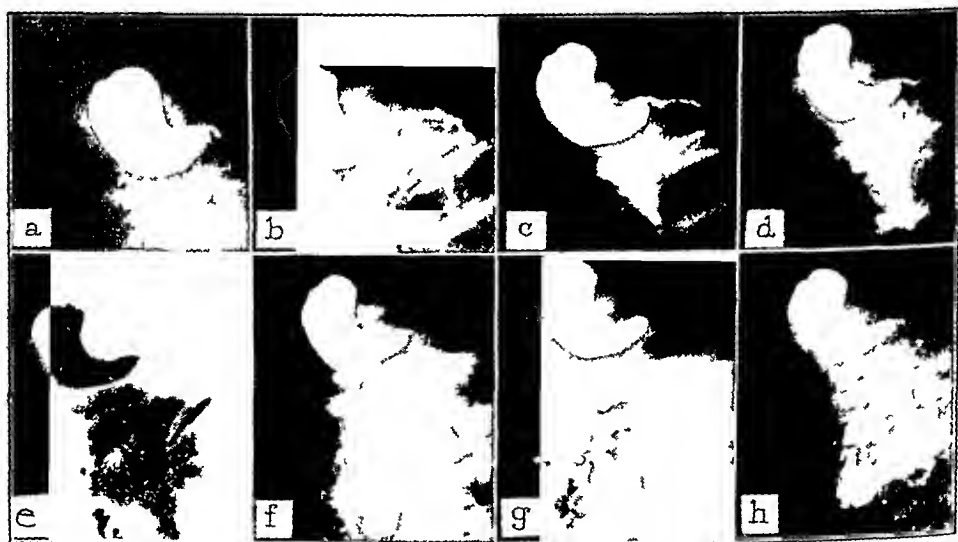


Fig 5—The emptying of the normal gallbladder of the dog at frequent intervals following the ingestion of a meal rich in fat, *a*, control, *b*, after five minutes, *c*, after fifteen minutes, *d*, after thirty minutes, *e*, after forty-five minutes, *f*, after one hour, *g*, after two and a half hours, and *h*, after three and a half hours

tion for the production of such pathologic changes, it has been noted that the gallbladders are practically devoid of change from two to three weeks after the injection (fig 5)

## ROENTGEN OBSERVATIONS

The series of animals was divided into three groups. The first group included the animals which received rose bengal and were subsequently given a mixture of egg yolk and cream four hours prior to operation. The duodenum was explored for any evidence of the dye, the gallbladder was aspirated and an equivalent amount of iodized oil was injected. The animals were then given a second meal of egg yolk and cream from six to eight hours after exploration, animals that

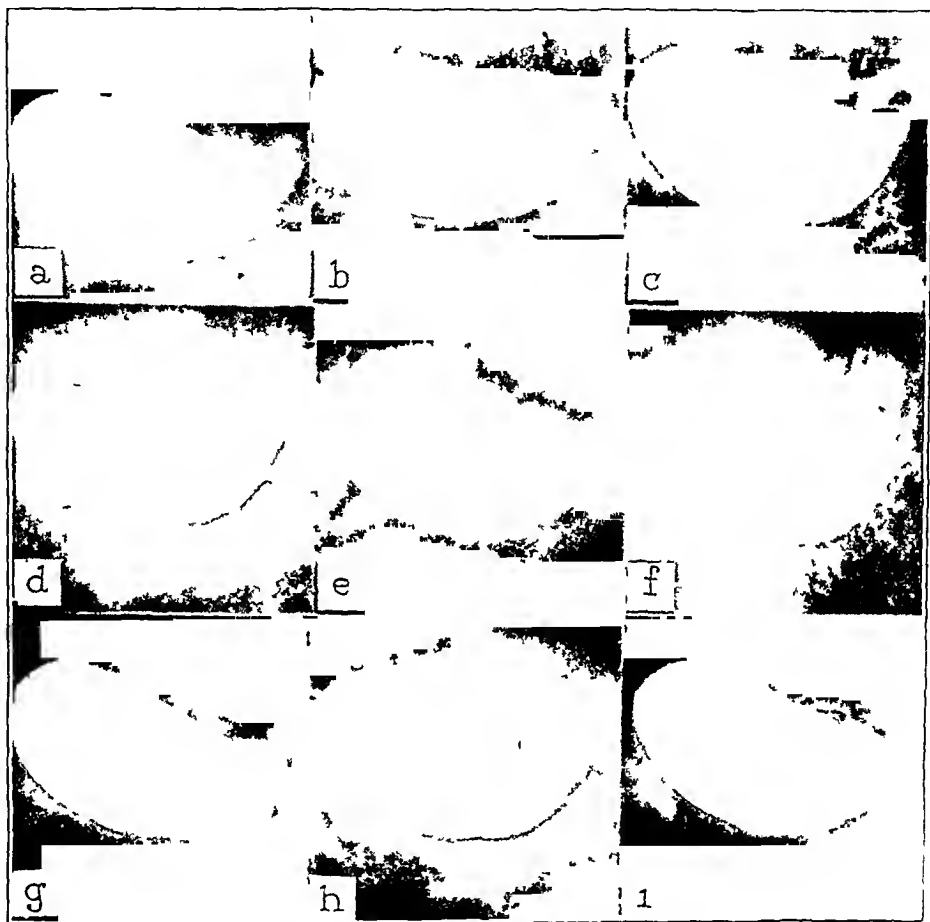


Fig 6—A case of cholecystitis graded 4, following the ingestion of a meal rich in fat. Emptying of the gallbladder did not occur, *a*, control, *b*, after five minutes, *c*, after fifteen minutes, *d*, after thirty minutes, *e*, after forty-five minutes, *f*, after one hour, *g*, after two and a half hours, *h*, after three and a half hours, and *i*, after twenty-four hours.

appeared ill or that did not retain the fat meal were discarded. Roentgenograms of the gallbladder were taken at fifteen to thirty minute intervals for from three and a half to four hours and in some instances even longer. In no instance in the group of gallbladders with lesions graded 1, 2 and 4 was there any evident of emptying (fig 6). Nevertheless the

gallbladder showed tonic changes, as evidenced by its contour. Frequently, two hours after the administration of the fat meal, the outline of the gallbladder became decidedly spherical, and its two linear dimensions approached one another. This would seem to indicate that an attempt had been made by the musculature of the gallbladder to reduce its content. These tonic changes, however, disappeared after from ten to twelve hours, the gallbladder then appeared normal but did not show evidence of having emptied. It may be noted that the same cycle is also followed in the gallbladder of the intact animal, and one is able to prognosticate, from early observations of its contour following the ingestion of a fat meal (fig 7), whether or not such a gallbladder is likely to empty. The original plan was to observe whether the gall-

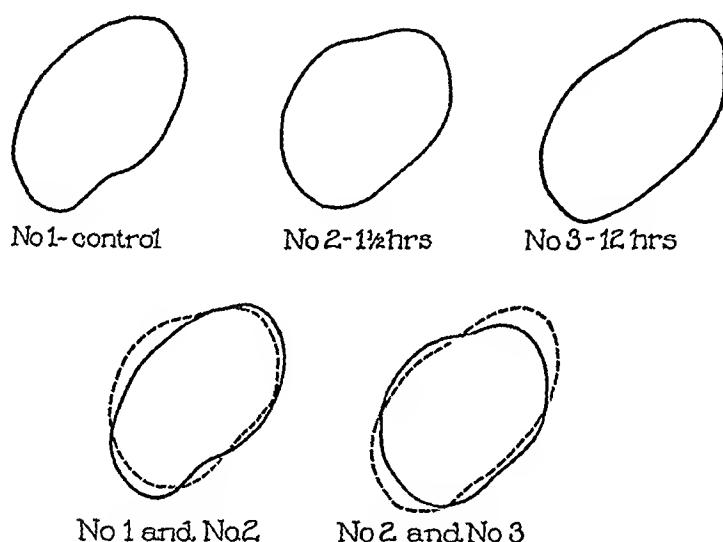


Fig 7—A case of cholecystitis graded 2 at frequent intervals after the ingestion of a test meal. Tonic changes of the wall of the gallbladder may be noted

bladders emptied over a four hour period. Some gallbladders were observed twelve, twenty-four, forty-eight hours and even a week after the repeated administration of a meal rich in fat as well as a regular laboratory diet, and emptying did not occur. This became all the more significant when it was found that after the injection of iodized oil into a normal gallbladder, the gallbladder emptied completely within twelve hours after the animal had been placed on a kennel diet (figs 8 and 9).

The second group differed only slightly from the first group, and, although egg yolk and cream were administered before and after the operation, rose bengal was not given, nor was the duodenum explored in any case. The group included cholecystitis graded 1, 3 and 4 without other pathologic changes elsewhere in the abdomen. In cholecystitis graded 3 and 4 there was, as usual, no evidence of any emptying. The

characteristic change in the tonicity of the wall of the gallbladder occurred, as had been observed frequently in other animals. In a case of cholecystitis graded 1 in the group in which a few lesions were confined entirely to the fundus of the gallbladder, it was found that one and a half hours after the ingestion of a meal rich in fat, a small amount of iodized oil had been forced out of the cystic duct and into the common bile duct. Three hours later, however, there was only an accumulation within the common bile duct of the iodized oil that had



Fig 8—Emptying of the normal gallbladder after the dog was placed on the regular kennel diet. *a*, control, *b*, after twelve hours.

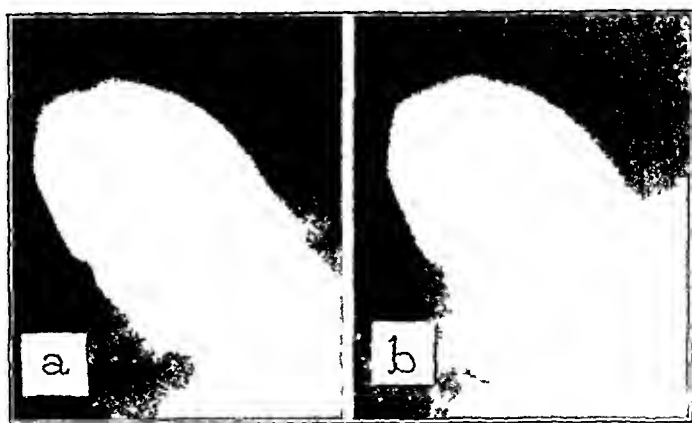


Fig 9—A case of cholecystitis graded 3. The animal was placed on the regular kennel diet for one week without showing any evidence of emptying of the gallbladder. *a*, control, *b*, after one week.

previously been expelled. Furthermore, roentgenograms of the gallbladder taken twenty-four hours later, after the animal had been on a kennel diet, showed that, although the gallbladder had completely regained its tonus, there was no indication of additional emptying. It is surprising in this respect how few lesions are necessary to interfere with the normal emptying mechanism in such gallbladders. However, the degree, extent and site of the lesions in this instance may easily

explain the observations. It is not assumed that all normal gallbladders empty completely from three to four hours after the ingestion of a meal rich in egg yolk and cream any more than it is felt that all diseased gallbladders produced by such chemical means do not partially empty under such conditions. It is assumed, however, that most normal gallbladders will show at least some evidence of emptying after a fat meal, on the other hand, only one instance has been encountered wherein a diseased gallbladder as described ever showed evidence of emptying. It must be remembered that occasionally cholecystograms are reported negative as regards lesions of the gallbladder, when at operation the viscus is found to be completely filled with stones. Although the analogy is only slightly divergent, the question of a dependable therapeutic test regarding the presence or absence of a lesion is closely akin, so far as the occurrence of irregularities is concerned.

In group 3, cholecystitis graded 2, 3 and 4 was observed. The animals were explored following the production of the lesions of the gallbladder, the bile was aspirated and an equivalent amount of iodized oil was injected. Twenty-four hours later the animals were given a meal rich in egg yolk and cream, and roentgenograms of the gallbladder were taken at frequent intervals thereafter. Although there was no evidence of any emptying of the gallbladders in which cholecystitis was graded 2 and 3, there were observations in one case of cholecystitis graded 4 in which the gallbladder emptied slightly following the test meal.

#### SUMMARY

The intravenous injection of varying amounts of eusol has resulted in the production of a high percentage of acutely inflamed gallbladders. The effect of the specific chemical cholecystitis on the emptying of the gallbladder was studied in a series of ten animals. Direct observations, as well as roentgenograms, were made of the diseased gallbladders following the administration of a meal rich in egg yolk and cream. Only one instance has been encountered wherein an acutely inflamed gallbladder, produced by this means, has shown any evidence of emptying. The observations appear to indicate that the acutely inflamed gallbladder does not empty after the usual test meal.

# THE MANAGEMENT OF GIANT CELL SARCOMA OF THE VERTEBRAE

REPORT OF A CASE WITH CURE AFTER FIVE YEARS \*

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PHILADELPHIA

Bone tumors of the epulis type are generally considered benign. At times however the growth invades the contiguous tissues, recurrences are common, metastases being reported by Gross,<sup>1</sup> Coley,<sup>2</sup> Stewart,<sup>3</sup> and others, cachexia is an accompaniment to extension and recurrence (64.7 per cent in the cases reviewed).

While these statements may be considered questionable by those who regard all tumors of the giant cell type as falling in one category, i. e., the benign, they are apparently facts when considered in relation to this type of growth where it invades the vertebrae. The following is an epitome of twenty-eight cases reported in the literature. The average age of the patients was 22.2 years, 46 per cent were below the age of 20 and 80 per cent below 30. Sixty-five per cent of the patients were males. Trauma was mentioned as a causative factor in 33.3 per cent. Pain was severe at the site of the lesion in 55 per cent and was referred in 33.3 per cent. Paralysis of the lower extremities was present in 26 per cent, weakness in 18, anesthesia in 26, and abnormal reflexes in 33.3 per cent. A mass was visible in 75 per cent, and kyphosis was present in 18 per cent. The roentgen diagnosis was correct in 41 per cent of instances, incorrect in 11, and in 48 per cent the roentgenographic report was absent in the protocol.

There were eight deaths, in all, a mortality of 28.5 per cent, two of the patients who died were not operated on, of the twenty-four on whom operation was performed, six died, a mortality of 25 per cent. Three patients died during the immediate operative period, two (cases

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\* Submitted for publication, Feb. 3, 1930.

\* From the Department of Surgical Research and Pathological Department, Temple University.

1 Gross, quoted by Coley.

2 Coley, W. B. *Ann. Surg.* **79**: 321 and 561, 1924.

3 Stewart, M. J. *Lancet* **2**: 1236 (Nov. 28) 1914.

25 and 18) of hemorrhage and one (case 23) of infection, in three of the twenty-four cases in which operation was performed, there were recurrences at the time of death, in the two cases in which operation was not performed, metastasis developed

#### RECURRENCES AND METASTASIS

*Recurrences*—There was a definite history of recurrence in eleven cases. A follow-up record could not be found in four cases, and four other patients had been under observation too short a time to determine definitely whether or not recurrence would have taken place, the average of the latter was seventy-six days. In those cases in which operation was performed, the minimum time between operation and the patient's discharge from the hospital was twenty-three days and the maximum five months, an average of eighty-five days. As there was a recurrence in case 17 after four years and a definite recurrence in case 2 after four, and probably another after ten years, we believe that the four cases previously mentioned should not be included in estimating the possible percentage of recurrence. If we deduct these eight cases and the three cases that proved fatal during the immediate operative period, there is a percentage recurrence of 64.7 per cent (eleven of seventeen).

*Metastasis*—While absolute evidence (microscopic report) that metastasis had taken place was wanting, a review of cases 8 and 9 would seem to indicate that such was the case.

#### EVALUATION OF THERAPEUTIC PROCEDURES

*Exploration of Growth*—In five patients, all of whom had recurrence, the growths were explored, two died as a result of the disease and one was unimproved, mortality, 40 per cent, recurrence, 100 per cent, unimproved, 60 per cent, cured, 40 per cent.

*Incomplete Removal*—This procedure was used in eleven cases with the following results: five recurrences and two deaths, no improvement, one case, this shows a mortality of 18 per cent, recurrences, 45 per cent, lack of improvement, 27 per cent, cures, 73 per cent.

*Complete Removal*—Complete removal was performed in five cases with the following results: two deaths and three recurrences, with apparent recovery in the latter, this shows a mortality of 40 per cent, recurrences, 60 per cent, cures, 60 per cent.

*Complete Removal and Laminectomy*—This procedure was performed in case 14. There was no history of recurrence but the patient had not improved at the end of eighteen months.

*Complete Removal with Subsequent Implantation of Radium at Operative Site*—This procedure was used in case 12. The patient was well at the end of three years, with no recurrence.

*No Attempt at Removal, Insertion of Radium Directly Into the Growth*—In a case in which this type of procedure was followed, there were no recurrences. The patient was well at the end of five years (See case report).

*Erysipelas and Prodigious Toxins (Colley's)*—This treatment was used in seven cases. In cases 21 and 27 it was the only therapeutic agent used, both patients recovered and had no recurrences. In five, it was used after partial removal of the growth. Three of the five patients had recurrences (cases 4, 5 and 20), but only one was not improved (case 5).

### CONCLUSIONS

It would seem that we are justified in drawing the following conclusions from the preceding review:

1. Giant cell tumors of the vertebrae should not be considered benign as compared with giant cell tumors of bone elsewhere.

2. While there is a tendency for them to regress normally they also possess the tendency to metastasize rarely, to recur commonly and to produce cachexia invariably.

3. The proximity of the spinal cord and nerve roots interfere with radical measures (operation). In a percentage of cases the growth begins in the body of the vertebra. This makes complete removal impossible. Regardless of where the lesion originated, removal is usually associated with profuse hemorrhage, necessitating packing, which increases the possibility of infection.

4. Exploratory operation, curettage, partial or complete removal evidently stimulates these abnormal cells to further activity. In over half of the cases (52.4 per cent) there were local recurrences.

5. Part of the high mortality is due to the improper interpretation of the x-ray plate. If the bodies of the vertebrae are affected, extension of the disease is rapid, the intervertebral disks are clear and early symptoms of a lesion of the transverse cord present themselves one should suspect a malignant condition.

6. The best treatment for this type of tumor is the insertion of radium into or near the growth with as little trauma as possible. Giant cells are peculiarly susceptible to the radium rays, the maximum and minimum doses are appended. The closed method of operation should be used because of the possibility of infection.



## REPORT OF A CASE

*History*—N. M., a woman, aged 20, had an unimportant family and previous history. She first menstruated when 15 years of age. Her menstrual periods were regular, at twenty-eight day intervals of five days' duration, and painless. There was no change in the character of the flow throughout her illness. At the age of 17, while walking down stairs, she slipped, and in order to regain her balance she quickly threw her shoulders back. This was accompanied by a sharp pain to the left of the lumbar spine, followed by a constant pain in this region, which was so severe at night that it interfered with sleep. It was referred to the posterior and lateral aspects of the left thigh and muscles of the calf of the leg, and confined her to bed for seven days. She stated that a lump appeared to the left of the lumbar spine about the size of a hen's egg about two weeks after the supposed injury. In October, 1924, after three years, she noticed that her left leg was much smaller than the right, and that she was unable to extend her leg and foot, this was associated with a feeling of numbness in the posterior

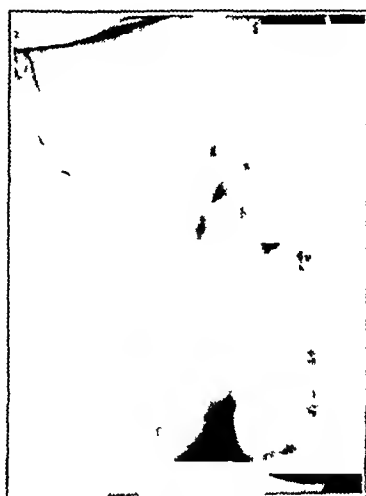


Fig 1—Before operation, the spinous processes of the second and third lumbar vertebrae are displaced to the right, the oval mass is seen below and to the left

tibial region. During the following month she consulted Dr. L. O. Davis, who advised a roentgen examination.

*Physical Examination*—Examination revealed an emaciated woman, aged 20, who weighed 70 pounds. The temperature was 98.6 F, the pulse rate 120. Examination of the head showed no gross abnormalities. The neck was normal. The chest was poorly developed with limited expansion in the apex of the left lung but no abnormal pulsations. The breath sounds were normal, except for questionable râles in the apex of the left lung. The area of cardiac dullness was normal, the heart sounds were strong and regular, and no murmurs were present. The abdomen was scaphoid, with no area of tenderness present, but the recti seemed to have plus tension. No abnormal masses were palpated. Inspection of the postdorsal and lumbar regions revealed a moderately prominent, oval-shaped mass to the left of the lumbar spine, about 8 cm in the horizontal direction and raised 2.5 cm from the surface; it was firm and regular in outline, apparently fixed to the spinous processes, and was not tender. The skin overlying the growth was of normal color and moved freely over the mass.



Fig 2—Nov 17, 1924, before operation The arrows indicate the extent of the tumor, the bodies of the second and third lumbar vertebrae being markedly involved

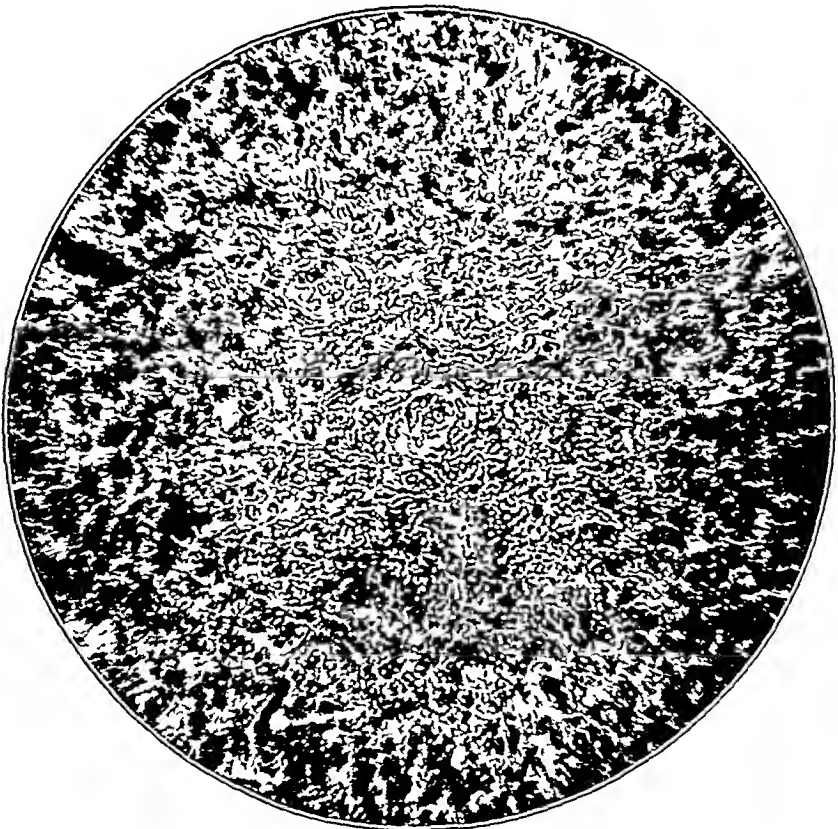


Fig 3—High power photomicrograph of the tumor Note the compact stroma and giant cells with the oval nuclei in the center of the illustration



Fig 4—Jan 12, 1925, eight 125 mg radium needles have been placed in the tumor mass about 15 cm distant from the spinal cord. Two insertions were made at six week intervals, making a total of 4,800 mg hours of radiation.



Fig 5—May 22, 1925, four months after the first and three months after second radium implantation. Note the increased density and diminution in the size of the mass.



Fig 6—June 21, 1928 three years and five months after the first implantation

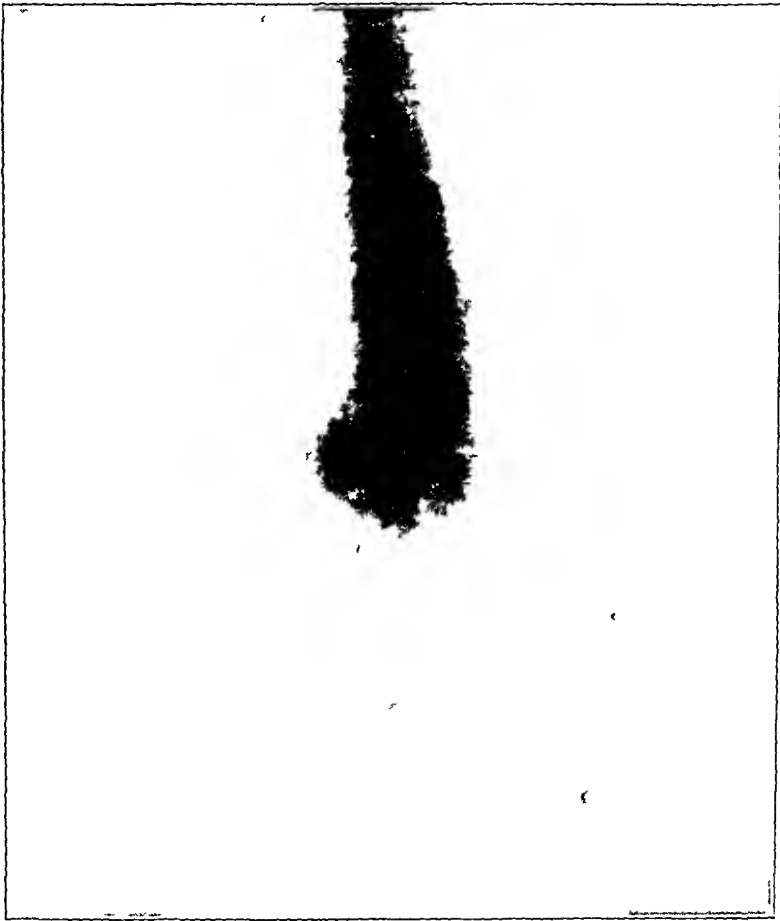


Fig 7—March 8, 1929, four years and three months after implantation  
Further diminution in the size of the growth with increased density is seen  
The patient is married and attending to housework

Case	Reporter and Reference	Age and Sex	Previous History Trauma or Tuberculosis	Duration of Pain	Referred Pain	Paralysis	Anesthesia	Mass
1	Manheimer, F Beitr z klin Chir 72 741, 1911	16 F	Not mentioned	Not mentioned	Lower extremities	No cord involvement	Not mentioned	Size of a fist at level of second lumbar vertebra
2	Sick Personal communication to Manheimer	M	Not mentioned	Not mentioned	Sciatic nerve and left lumbar region	Not mentioned	Not mentioned	Fluctuating tumor between thirteenth and twelfth dorsal vertebra on abdominal side, mass had a bony capsule
3	Ashurst reported by Dean Lewis	14 M	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Right loin, 6 weeks' duration
4	Harmer Boston M & S J, 1915, p 61	16 M	History of trauma, 3 months before entrance to hospital patient fell striking spine	Pain and tenderness	Lower dorsal region and to occiput	Weakness in right knee	Loss of sensation over exterior and anterior surface of right thigh, 2 weeks	Size of hand in the subcostal region of the tenth dorsal vertebra
5	Minter reported by Dean Lewis	31 M	No history of trauma	Girdle	Not mentioned	Weakness in legs, paralysis with sphincter disturbance below fifth dorsal vertebra	Anesthesia in legs, later below fifth dorsal vertebra	Not mentioned
6	Folhs reported by Dean Lewis	40 M	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Fluctuating mass between the sixth and twelfth dorsal vertebrae
7	Kesmodel Am J Roentgenol 8 573, 1921	43 M	No	12 months, back not relieved by rest	Pain in left leg	Weakness, atrophy of left leg	Not mentioned	Not mentioned
8	Raseh Hygiene 84 769 (Oct) 1922	31 F	Not mentioned	No early pain	Limbs felt heavy and clumsy	Spontaneous twitching of legs	8 months after onset in abdomen and hips, gradually progressing downward	Fluctuating mass at tenth dorsal vertebra

# Cell Sarcoma of the Vertebrae

Kyphosis	Reflex	X Ray	Operation	Post operative Irradiation	Pathologic Report	Outcome and Comment
Not mentioned	Negative	Destruction of transverse process of second lumbar vertebra	Tumor removed as thoroughly as possible	Not mentioned	Osteoid spindle cell sarcoma with myomatous areas containing giant cells	Observed only 5 months, treated with 0.01 Gm of atoxyl intravenously every other day for 46 days appeared well at the end of 5 months
Not mentioned	Not mentioned	Distmet shadow between iliac crest and twelfth dorsal vertebra	Partial removal with no improvement, potassium arsenate given patient well 4 years later	Not mentioned	Giant and mixed cell fibrosarcoma	Recurrence after 4 years 10 years later patient alive but not well
Not mentioned	Not mentioned	Involvement of fourth and fifth lumbar vertebrae roentgenogram 17 months after cessation of treatment revealed shadow of dense bony tissue	Incision wound packed with gauze, mass increased in size after operation broke down 9 months later then because of bony hardness	Not mentioned	Giant cell sarcoma	Coley's fluid given on second, third and fourth days, increased to 26 cc at a dose accepted for army later
Depression of tenth dorsal vertebra	Ankle clonus, Oppenheim's reflex on right side	Showed recurrence after second operation negative before	June 1912, exploratory incision revealed a bluish rather tense but fluctuant mass beneath muscles of the back, removed and wound packed with gauze	Not mentioned	Giant cell sarcoma	Treated with mixed toxins for 7 months injections every other day then twice each week reaction severe rapid recurrence of the tumor 5½ by 3½ by 2 inches associated paresis of right leg June 1913 no mass June, 1914 another operation because of recurrence bone cyst found patient well 2 years later
Not mentioned	Not mentioned	Negative	First, incomplete removal Coley's toxins given complete paralysis recurrence with complete block of spinal canal, laminectomy of fourth and fifth dorsal vertebrae	Yes	Giant cell sarcoma	Recurrence final outcome not mentioned
Not mentioned	Not mentioned	Not mentioned	Complete removal with recurrence in 4 months larger than first	Not mentioned	Giant cell of epulis type	No follow up
Lumbar scoliosis	Knee jerks absent on left	Negative except for slight hypertrophic changes	Complete removal	Not mentioned	Fibrosarcoma with giant cells	Follow up not mentioned
Kyphosis of eighth and ninth dorsal vertebrae tenth depressed	Pitella on right absent	Diagnosis of tumor of tenth dorsal vertebra no treatment	First, exploratory incision showed necrosis	Not mentioned	Giant cell tumor with transverse myelitis	Death lumbar puncture bloody air insufflation of spine questionable metastases in pleural cavity



Case	Reporter and Reference	Age and Sex	Previous History Trauma or Tuberculosis	Duration of Pain	Referred Pain	Paralysis	Anesthesia	Mass
9	Kono N Sei Kwa M J Tokyo, 44 18 1927	29 M	Not mentioned	Rapid development, 6 months	Not mentioned	Not mentioned	Not mentioned	Mass the size of a child's head
10	Madelung Munche med Wehnschr 56 479, 1909	19 M	Trauma, struck in back 14 years previously	Not mentioned	Not mentioned	Yes	Yes	Not mentioned
11	Shumann reported by Dean Lewis	27 M	Not mentioned	Pain in back, 3 months	Not mentioned	Paraplegia	Not mentioned	Second lumbar vertebra
12	Lewis, Dean J A M A 83 1224 (Oct 18) 1924	7 F	Not mentioned	Night cries for 3 weeks	Stomach	Wabbling gait, weakness of muscles, lower extremities	No anesthesia	Not mentioned
13	Kesmodel, Karl F Am J Roentgenol 8 573, 1921	16 M	Fell 3 months previously	3 months	Backache	Yes	Over right thigh	Swelling, depression over the tenth dorsal to the right of vertebra
14	Cushing reported by Dean Lewis	13 F	Not mentioned	Not mentioned	Not mentioned	Both legs, hipsoas	Below eleventh dorsal vertebra, epiritic 2 inches above	Between tenth and eleventh dorsal vertebrae
15	Cushing reported by Dean Lewis	16 M	Both	Lower dorsal and lumbar vertebrae	No referred pain	Redness of legs	Not mentioned	Tender 12 months after injury
16	Cushing reported by Dean Lewis	13 F	Not mentioned	6 months, lumbar vertebra	Left leg and foot, then both legs	Not mentioned	No anesthesia	Not mentioned
17	Madelung reported by Dean Lewis	25 M	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Mass from twelfth dorsal vertebra to iliac crest
18	Thompson reported by Dean Lewis	24 M	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Fungating mass over sacrum

*Cell Sarcoma of the Vertebrae—Continued*

Kyphosis	Reflex	X Ray	Operation	Post operative irradiation	Pathologic Report	Outcome and Comment
Not mentioned	Not mentioned	Not mentioned	No	Not mentioned	Rieb in giant cells, also spindle cells, part polymorphous clears	Death, metastasis in ribs bilateral, chondromyxoid endothelioma, probably metastatic development from parotid in temporal region, 10 years' duration, size of hen's egg, reduced by radium, not a metastasis from vertebrae
Not mentioned	Not mentioned	Not mentioned	Curettage of third and fourth cervical cavity size of hen's egg	Not mentioned	Giant cell myeloid sarcoma	Well 3 months after curettage, complete disappearance of symptoms
Not mentioned	Not mentioned	Not mentioned	Complete removal with recurrence of tumor in 8 months, size of man's head, patient readmitted 9½ years later ossification had taken place	Not mentioned	Giant cell	Bladder and rectal disturbance persisted paraplegia
Not mentioned	Bilateral Babinski sign, ankle clonus no abdominal reflex	Rarefaction of right half of body of fourth dorsal vertebra	Laminectomy of second, third, fourth and fifth dorsal vertebrae, mass removed, dura not opened, 4 weeks later 50 mg of radium placed for 18 hours in region formerly occupied by tumor, 900 mg	X ray same time	Frangible vascular mass extending 2 inches along cord, giant cell sarcoma	After 3 years child apparently normal
Not mentioned	Ankle clonus, Oppenheim's reflex	No preoperative roentgen examination	Exploratory operation, encapsulated liquid containing broken down tissue	Not mentioned	Giant cell sarcoma	No improvement following operation
Not mentioned	Lost knee jerks, achilles jerks present on both sides, but plus on the left	Not mentioned	Laminectomy and extirpation	Not mentioned	Giant cell sarcoma-extradural spindle cells	Automatic bladder and rectum protective reflex 9 months after operation no voluntary return of paralyzed muscles but reflex present, incontinence 18 months later sensation and motion had not returned
Not mentioned	Not mentioned	Roentgenogram positive, third to fifth lumbar vertebrae	Partial removal of tumor at third to fifth lumbar vertebra tumor passed off to right	Yes	Giant cell bony tissue between cartilage and bone	No follow up
Not mentioned	Not mentioned	Not mentioned	Partial removal of tumor in sacral region	Not mentioned	Giant cell	Death 4 years 4 months after operation, rectal disturbance, 6 weeks loss of weight and urgency
Not mentioned	Not mentioned	Not mentioned	Extirpation	Not mentioned	Giant cell myxomatous tissue	Recurrence from 4 to 6 years after operation no metastases but local recurrences, death
Not mentioned	Not mentioned	Not mentioned	Tumor removed hemorrhage profuse	Not mentioned	Giant cell	Death

Case	Reporter and Reference	Age and Sex	Previous History Trauma or Tuberculosis	Duration of Pain	Referred Pain	Paralysis	Anesthesia	Mass
19	Leahe reported by Dean Lewis	Not mentioned	Yes, trauma 5 years previously	Not mentioned	Not mentioned	Left leg	Not mentioned	No mass
20	Greenough, Simmons and Harmer	16 M	Trauma 3 months before symptoms	3 months	Not mentioned	Not mentioned	Not mentioned	Thickening
21	Harmer, T W Brit M J 172 443, 1915	21 M	Not mentioned	Not mentioned	Not mentioned	Legs, rectum and bladder	Not mentioned	Yes
22	Reported by Thomas Brit M J 172 443, 1915	F	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned
23	Klebs Die allgemeine Pathologie, 1889 part 2, p 732	23 F	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned
24	Volkmann, R Deutsche med Wehnschr, 1876, p 281	23 F	Not mentioned	Sacrum and rectum 1 year	Not mentioned	Weakness	Not mentioned	Mass of 9 months' duration, for past 6 months, size of egg
25	Gussenbauer, C Teischr f Heilk 11 473, 1890	33 F	Not mentioned	Continuous sacral pain after child birth	Not mentioned	No	Not mentioned	Sacral vertebrae
26	Peham, H Deutsche Wehnschr 45 241, 1897	17 M	Not mentioned	Sudden pain in sacral region	Not mentioned	Not mentioned	Not mentioned	Mass in sacral region
27	Colby reported by Dean Lewis	21 M	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Soft pillow
28	Bower, Clark and Davis	20 F	Yes, 3 years previously	3 years	To posterior tibial region	Incomplete paralysis of muscles supported by sciatic nerve	No	Yes to left of lumbar spine

*Cell Sarcoma of the Vertebrae—Continued*

Kyphosis	Reflex	X Ray	Operation	Post operative Irradia- tion	Patho- logic Report	Outcome and Comment
Not men- tioned	Not men- tioned	Not mentioned	No operation	Not men- tioned	Necropsy showed a hemorrhagic mass between first and second lumbar vertebrae, which developed from transverse processes	Seven months prior to death patient lost control of bladder and rectum, bed sores developed, death
Not men- tioned	Not men- tioned	Small tumor of third lumbar vertebra arising from lateral surface of spinous process	Partial excision	Not men- tioned	Giant cell tumor, many small giant cells, stroma, fibrous type	Local recurrence in wound immediately, received Coley's toxin treatment by injection direct into tumor for 7 months, 62 injections, tumor sloughed out, wound healed in 2 years, later tumor appeared in scar, no tumor tissue found well 8 years after operation
Not men- tioned	Not men- tioned	Not mentioned	No operation mass extended from eighth dorsal to third lumbar vertebrae, 0.3 inches either side of vertebrae	Not men- tioned	Giant cell sarcoma	Treated as Pott's disease for several months, Coley's toxin given 3 months with intervals of rest, maximum dose, 3 minims, patient entirely well from 7 to 8 months later no recurrence after 12 years
Not men- tioned	Not men- tioned	Not mentioned	Partial extirpation	Not men- tioned	Giant cell sarcoma tumor of sacrum	Well 1½ years after Coley's fluid given
Not men- tioned	Not men- tioned	Second cervical vertebra, began left lateral process	Exploratory	Not men- tioned	Giant cell sarcoma	Death in few days, from sinus thrombosis and purulent meningitis
Not men- tioned	Not men- tioned	Not mentioned	Removal complete	Not men- tioned	Giant cell sarcoma	Patient discharged 6 weeks later complaining of painful defecation which gradually subsided
Not men- tioned	Not men- tioned	Not mentioned	Attempted removal	No	Giant cell sarcoma	Died from hemorrhage during operation, tumor involved fifth lumbar vertebra no metastases
Not men- tioned	Not men- tioned	Not mentioned	Exploratory operation for suspected cancer third sacral vertebra	Not men- tioned	Giant cell sarcoma	Discharged 23 days after operation, no follow up
Not men- tioned	Not men- tioned	Not mentioned	No operation	Not men- tioned	Giant cell sarcoma	Only treatment, Coley's fluid given well 2 years later
Yes	Patellar reflex absent Babinski?	Sarcoma of bodies of second and third lumbar vertebrae	Biopsy and insertion of radium needles	Surface application of radium	Giant cell sarcoma	In good health after 5 years

The right lower extremity was normal. The reflexes were present, and there were no areas of anesthesia. The muscles of the left lower extremity were markedly atrophied, particularly the posterior tibial group. A foot drop was present. The patellar reflex was absent, and there was a questionable Babinski sign. There were no areas of hyperesthesia or anesthesia. Heat and cold were recognized on any part of the extremity. There was paralysis of the quadriceps extensor, tibialis anticus, extensor longus digitorum and extensor longus hallucis and marked weakness of the hamstrings and posterior tibial group.

Urinalysis gave negative results. Examination of the blood revealed hemoglobin, 62 per cent, erythrocytes, 3,790,000, leukocytes, 7,100, polymorphonuclears, 74, small lymphocytes, 24, large lymphocytes, 1, transitionals, 1.

The roentgen examination by Dr. G. C. Bird showed an evidently sarcomatous mass involving the bodies of the second and third lumbar vertebrae.

On Nov. 28, 1924, with the patient under gas anesthesia, a 10 cm. semilunar incision was made, beginning at the upper border of the spinous process of the first lumbar vertebra and extending downward to the left and to the upper border of the fourth lumbar vertebra. The skin flap was reflected, the lumbar fascia divided and the erector spinae muscle retracted. The transverse processes were softened and replaced by a bluish-red calcareous material which bled profusely. The mass was about 7 by 5 by 3 cm., the center of greatest density being opposite the spines of the second and third lumbar vertebrae, the pathologic process having practically accomplished a transverse section. A biopsy was performed, and the pathologic report was as follows: Several small pieces of soft reddish tissue and a few spicules of bone were seen. The section showed a stroma of spindle cells of varying density inclosing numerous thin-walled capillaries and blood spaces unlined by endothelium. Many giant cells were present in the stroma, characterized by an acidophilic cytoplasm and averaging from ten to twelve clear oval nuclei centrally located. A diagnosis of giant cell sarcoma was made.

Eight needles, each containing 125 mg. of radium, were inserted into the center of the mass. The fascia was closed with interrupted chromic catgut, the skin with interrupted horse hair sutures. A roentgenogram was made with radium needles in situ to determine the exact position of the element in relation to the cord. The roentgenogram showed them to be from 0.5 to 1 cm. distant. The needles were removed in twenty-four hours, a total of 2,400 mg. hours of radiation having been given. The wound healed primarily, the sutures were removed on the fifth day. Two days after operation, contraction of the tibialis anterior was noted. A plaster of Paris cast was applied on the seventeenth day after operation, and the patient was discharged from the hospital on the twenty-first day. Improvement was rapid, and on her return to the hospital on February 8, there was complete return of power in all the paralyzed muscles, and the reflexes were normal. She had gained about 4 pounds (1.8 Kg.). The pulse rate was 112, the temperature normal. The urinalysis gave negative results. The blood count was hemoglobin, 62 per cent, erythrocytes, 3,460,000, lymphocytes, 8,400, polymorphonuclears, 72, small lymphocytes, 26, large lymphocytes, 1. On February 9, the same operative approach being used, eight 125 mg. needles were again inserted into the growth for twenty-four hours. A roentgenogram was made with the needles in position. The mass was smaller, partially calcified and not as hemorrhagic as at the previous operation. The wound healed normally, and the patient was again discharged from the hospital twelve days after the operation. A cast was not applied. A roentgenogram of the chest was negative. The patient continued to improve, and was again admitted to the

hospital on May 21, 1925, at which time radium was applied to the mass 2 cm distant from the growth, 100 mg for twenty hours, making a total of 2,000 mg. This was repeated on Aug 25, 1925. A roentgenogram at this time showed that a large mass of osseous tissue had replaced the tumor mass. The last application of radium was made on Feb 11, 1926 (2,000 mg). The patient's general condition was excellent. The contraction of the previously paralyzed muscles was practically normal, and there was but a slight degree of atrophy present. She had no pain. The pulse rate was 100.

*Subsequent History*—Five years and one month after the onset of symptoms and five years after radium implantation, the patient is in good health. Disregarding the advice of her family physician, she was married (September, 1929) and is doing her own housework.

NOTE—Since this manuscript went to press, our attention has been drawn to an article by A. W. Adson (*Osteitis Fibroas Cystica of the Spine*, Surg Gynec Obst **46** 684, 1928) dealing with two cases in which pulpy, friable spinal tumors developed apparently following trauma. These cases were reported three years and three months, respectively, after the tumors were removed successfully.

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# THE EFFECT OF SPINAL ANESTHESIA ON THE CARDIAC OUTPUT \*

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The increasing recognition of spinal anesthesia as the method of choice in many operations has seemed to warrant an investigation into its physiologic effect. In this paper we present the results of a series of studies along this line. Since clinical experience has demonstrated that under spinal, as under other, anesthesia the state of the circulation is of primary concern to the surgeon, the first observations have dealt with the cardiac output and blood pressure.

Dogs were used in the experiment. One to two hours before the experiment was begun, morphine (from 10 to 15 mg per kilogram of weight injected subcutaneously) or barbitol (0.3 Gm per kilogram, intravenously) was given. Arterial pressure was measured by a mercury manometer, the cannula being inserted in the carotid artery. The cardiac output was determined according to the Fick principle, the technic being that employed by Harrison and Leonard<sup>1</sup>. The rubber mask designed by Blalock<sup>2</sup> was used to connect the animal to a Benedict spirometer. The Roth<sup>3</sup> recording device was used. Arterial blood was obtained from an exposed femoral artery, venous blood, from puncture of the right ventricle, as first done by Barcroft, Boycott, Dunn and Peters<sup>4</sup>. The oxygen contents of arterial and venous blood were measured in the Van Slyke-Neill<sup>5</sup> apparatus.

After the control observations had been made, the animal was turned on its side, and spinal puncture was done. The needles and technic were essentially the same as those used for this procedure in man. At first some difficulty was encountered in entering the spinal canal, but after a little practice the puncture was easily performed. It

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\* Submitted for publication, Feb 3, 1930

† From the Departments of Gynecology and Medicine, Vanderbilt University

1 Harrison, T R, and Leonard, B W. *J Clin Investigation* **3** 1 (Oct) 1926

2 Blalock, A. *J Lab & Clin Med* **12** 378, 1927

3 Roth, P. *Boston M & S J* **186** 457, 1923

4 Barcroft, J, Boycott, A E, Dunn, J S, and Peters, R A. *Quart J Med* **13** 35, 1919

5 Van Slyke D D, and Neill, J M. *J Biol Chem* **61** 523, 1924

was usually necessary to employ suction with a syringe in order to be certain that one had entered the cerebrospinal space, as spinal fluid frequently failed to drip from the needle. A solution of 1 per cent procaine hydrochloride and 0.1 per cent strychnine sulphate was used in some experiments and procaine in others. The doses used in most of the experiments were of the same order of magnitude as those employed clinically. In the later observations, the effect of larger doses was studied. The foot of the table was elevated in some experiments, but not in all of them. After the characteristic fall in blood pressure had developed, the cardiac output was again measured.

The results of these studies are shown in the table. No constant changes were observed in oxygen consumption or in the oxygen con-

*Effect of Spinal Anesthesia on Dogs*

Experiment Number	Control Period Before Spinal Anesthesia		After Spinal Anesthesia		Percentage Change	
	Minute Cardiac Output	Mean Arterial Pressure	Minute Cardiac Output	Mean Arterial Pressure	Minute Cardiac Output	Mean Arterial Pressure
3	2180	84	(a) 1980 (b) 1580	60 28	-9 -27	-29 -67
5	2720	138	(a) 3050 (b) 2540	96 110	+12 -6	-30 -20
7	2320	108	2230	66	-21	-39
8	2330	120	2100	70	-10	-42
10	1680	100	1340	66	-15	-34
11	1500	104	660	46	-56	-56
12	1140	116	800	84	-30	-28
13	1300	114	420	34	-68	-90

tents of the blood, and therefore the values for these functions are not presented. As can be seen in experiments 3 and 5, the blood pressure fell before the cardiac output decreased. In six of the eight experiments, the degree of diminution in blood pressure was greater than that in the cardiac output. When the decline in blood pressure was relatively slight (experiments 3a, 5a and 5b), the minute cardiac output usually remained at or nearly at a normal level. (Changes of 10 per cent or less cannot be regarded as significant, as this is approximately the limit of error of the method.) Greater diminution in arterial pressure (experiments 7, 8, 10 and 12) were usually followed by moderate decrease in the blood flow, and when the drop in arterial pressure was extreme (experiments 11 and 13) the cardiac output was also very low.

From the data it appears that in spinal anesthesia the initial change is, as would be expected, in arterial pressure, and that the venous return and output of the heart are affected secondarily. This sequence of events is just the opposite of that in hemorrhage. In this condition,



Blalock<sup>6</sup> has shown that the cardiac output decreases first and is already reduced by from one-third to one-half before a significant decline in mean arterial pressure occurs. These observations probably explain the well recognized clinical fact that a low blood pressure due to hemorrhage is a much more serious sign than a similar blood pressure in a patient under spinal anesthesia. These observations lend support to the views of Blalock,<sup>7</sup> who studied the effect of trauma on the spinal cord and found that a given lowering of blood pressure was accompanied by less diminution of cardiac output than was the case after hemorrhage. The same author<sup>8</sup> has recently shown that secondary shock due to muscle injury can be explained almost entirely by local hemorrhage within the traumatized area. It appears that the lowering of the blood pressure under spinal anesthesia is analogous to that occurring in primary shock or collapse or in ordinary syncope. Such an understanding of the mechanism of spinal shock may have therapeutic significance. *A priori*, since the peripheral resistance is primarily at fault, one would expect more value from vasoconstrictor drugs than in hemorrhage, a condition in which the circulatory blood volume, venous return and cardiac output are essentially affected.

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6 Blalock, A. Mechanism and Treatment of Experimental Shock, Arch Surg **15** 762 (Nov) 1927

7 Blalock, A., and Bradburn, H. B. Trauma to Central Nervous System Its Effects on Cardiac Output and Blood Pressure, Arch Surg **19** 725 (Oct) 1929

8 Blalock, A. Experimental Shock. The Cause of Low Blood Pressure Produced by Muscle Injury, to be published

# THE ETIOLOGY OF INTERSTITIAL AND MEDIAS- TINAL EMPHYSEMA

(EXPERIMENTAL PRODUCTION OF AIR EMBOLISM, ACUTE PNEUMO-  
THORAX, ACUTE PNEUMOPERITONEUM, INTERSTITIAL, MEDIAS-  
TINAL AND RETROPERITONEAL EMPHYSEMA) \*

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The term mediastinal and interstitial emphysema in our work is used to include not only the introduction of air into all the areolar tissues of the body, but also acute pneumothorax, acute pneumoperitoneum and air embolism. This condition has often been referred to as surgical emphysema because a good proportion of clinical cases develop after an injury which is usually treated by the surgeon.

The causes of interstitial emphysema as given by various authors may be summarized under the following groups:

1 Traumatic, namely, due to an injury of the lung produced by stab wound of the wall of the chest, a fractured rib or a needle during the induction of an artificial pneumothorax.

2 Sudden increase of the intrapulmonic air pressure resulting from physical strain such as coughing, childbirth or obstruction of the air passages by aspiration of foreign bodies.

3 Entrance of air into the fascial planes during operative procedures that cause an opening of the fascial planes and under certain conditions that allow the air to be sucked in.

4 Retroperitoneal emphysema caused by a perforation or an injury to the retroperitoneal surface of the colon or the duodenum or extension through the diaphragmatic openings from the mediastinum to the retroperitoneal areolar tissue.

5 Administration of general anesthesia by the closed method or the inflation method, in which the intrabronchial air pressure is increased. Lihenthal<sup>1</sup> noted such an emphysema in a patient who received a general anesthetic by the insufflation method, and in whom the air pressure was raised to 60 mm of mercury.

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\* Submitted for publication, Dec 31 1929

<sup>1</sup> From the Department of Surgery, College of Medicine, University of Illinois

1 Lihenthal, H. Thoracic Surgery, Philadelphia, W. B. Saunders Company, 1926, vol 1 p 250

Our interest in this work was aroused by an accidental production of the condition in a dog in a series of experiments on the etiology of pulmonary abscess<sup>2</sup> As we were introducing the infected blood and sputum into the lung through the bronchoscope, we noted that by the introduction of air into the lungs under suddenly increased pressure an interstitial emphysema was produced This condition was repeated at will in dead as well as in live animals, and our results were uniformly positive A careful study of the various underlying factors was therefore undertaken

#### METHOD

A small tube was inserted into the mouth or the trachea of a dog under ether anesthesia, and the air was blown in at known pressures The tracheal tube was large enough in diameter to allow the excess air to return to the mouth and come out In order to produce a sudden increase of intrapulmonic pressure, we compressed the floor of the mouth or the trachea, and for a known time we held the air in the lung This sudden increase of pressure, though momentary, was sufficient to cause interstitial emphysema In a series of experiments, the air was introduced through one source and removed at a different outlet Under such conditions the outgoing, as well as the ingoing, air pressure could be under control and thus various factors could be studied By means of a capillary microscope, Dr D M Olkon studied the capillary circulation of the skin under varying degrees of increased intrapulmonic pressure

#### EXPERIMENTS AND RESULTS

In the first series of experiments we made an effort to find out what happens when a blast of compressed air is blown into the lung With the dog under ether anesthesia, air was allowed to enter the trachea through a bronchoscope that was passed beyond the larynx With a compression of the trachea for from five to ten seconds, at times repeated two or three times, we could produce interstitial emphysema The sequence of events was as follows With the introduction of air under increased pressure, the respiration became shallow and in some cases stopped entirely, to be resumed again from one to five minutes later With the sudden blast, pneumothorax was produced and the diaphragm, which bulged downward, caused some distention of the abdomen As more air was blown in, the abdomen became distended considerably more, and the walls became drumlike on account of the pneumoperitoneum As the air finds its way through the inguinal rings and the cervical fascial planes, it escapes to the surface and extends to the neck, the floor of the mouth, the face and the retro-orbital space, causing an exophthalmos Very little air reaches the upper extremities From below through the inguinal rings the air finds its way through the

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2 Hedblom, C A , Joannides, Minas, and Rosenthal, S Pulmonary Abscess, An Experimental Study, *Ann Surg* 88 823 (Nov) 1928 Joannides, Minas The Etiology of Pulmonary Abscess, *Surg Gynec Obst* 47 449, 1928

fascial planes upward to the costal margin and spreads posteriorly to the opposite side of the abdominal wall. Anteriorly the air does not spread beyond the midline because the fascia is fixed, but it can travel posteriorly as no fixed points are present. If the emphysema is not marked, the dog may remain in this condition for several hours and then recover so that in from two to ten days no evidence of air is present. Most animals, however, died and at autopsy we found an acute tension pneumothorax with compression of the lungs. We also noted air bubbles at the hilus of the lungs at the point at which the parietal pleura joins the visceral pleura. It appears that this junction has a loose union with the lung, and air can easily escape at this point when the lung is injured. Bullae of air of varying sizes were noted in the lung. No doubt when the intrapulmonic pressure becomes increased, the pleura gives way and the air balloons up this loose portion of the pleura. In a study of the histology of the lung in the living dog, we noted areas in which there was an oblique or sagittal section of the smaller bronchus,<sup>3</sup> the inner half of which subdivided into its normal divisions but the outer half remained open and was covered only by the thin loose pleura. With each inspiration this area distended slightly more than the rest of the surface, and under increased intrapulmonic pressure the loose pleura separated more and a bulla of air was formed. It is ruptured bullae such as this, in addition to leakage of air from the mediastinal areolar tissue, that produce acute pneumothorax. The air bubbles in the mediastinum extend upward toward the cervical fascia and downward through the postesophageal areolar tissue to the mesentery and retroperitoneal tissues. At the hiatus esophagus of the diaphragm an anatomic study revealed the presence of a small inverted triangle, the sides of which were joined together by means of thin fibrous tissue.<sup>4</sup> Under increased pressure from above, the air finds its way through this opening into the abdominal retroperitoneal tissues and spreads along the root of the mesentery downward to the fascia of the iliopsoas muscle and out through the inguinal ring to the superficial tissues in the abdominal wall. At the region of the perirenal areolar tissues frequently a bulla will form which in turn ruptures and allows the air to escape into the free peritoneal cavity thus causing a pneumoperitoneum. When the air travels upward, it passes through the cervical planes and reaches the subcutaneous tissues of the chest. When the sublingual tissues

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3 Joannides, Minas, and Olkon, D. M. The Structure of the Alveolus Pulmonalis in the Living Dog. A Capillaroscopic Study, to be published. Joannides, Minas. Surface Stereomicroscopy of the Lung in the Living Animals, to be published.

4 Joannides, Minas. The Relation of the Hiatus Esophagus of the Diaphragm to the Stomach, *Arch. Int. Med.* **43**: 61 (Jan.) 1929, The Influence of the Diaphragm on the Esophagus and the Stomach, *ibid.* **44**: 856 (Dec.) 1929.

became distended with air, the tongue was pushed up from its bed, thus making it impossible for the dog to breathe. With an additional amount of air under pressure, the face swelled up, and finally the retrobulbar tissues of the orbit caused a marked exophthalmos. Examination of the heart and the general circulation revealed the presence of air in the blood stream. When the heart was opened, we found that in all the chambers the blood changed into a foamy mass, and air bubbles of varying sizes could be traced in the arterial as well as in the venous tree. Capillaroscopic studies by Dr. Olkon revealed the presence of microscopic air bubbles in capillaries of the heart muscle, the kidneys, the bladder, the stomach, the intestines, the brain and the skin.

The results of these experiments necessitated the explanation of the mechanics of several factors. 1. What causes the emphysema? Does it necessarily depend on the increased intrapulmonic pressure per se, or is it secondary to a tear in the lung tissue? 2. What causes death in these animals? Is it the acute tension pneumothorax, the air embolism, the pneumoperitoneum or the interstitial emphysema per se? 3. In the dogs that survive the shock of the experiment, what happens to the air in the tissues and the circulation? 4. How can these animals be saved after the syndrome develops? Would the animals survive if an outlet was made for the air through the skin, the thoracic (to relieve the pneumothorax) or the abdominal wall (to relieve the pneumoperitoneum)?

To determine the effect of the presence of air in the subcutaneous tissues, air under pressure was injected subcutaneously by means of a trocar. In this series, the dog was merely ballooned up and showed evidence of discomfort owing to the distention of the skin. The air was injected at the right inguinal region, but promptly traveled upward and spread throughout the whole body except the extremities. As soon as the trocar was removed, the air began to leak out through the opening made by the trocar. An attempt to suture that opening caused the air to leak out through the new openings made with the needle. The more incisions present in the skin, the quicker the air escapes from the interstitial tissues. If the animal is left alone the ballooning disappears, but crepitation remains and persists for from a week to ten days. Such an experiment was not sufficiently shocking to the animal to cause death. When the animal was killed, we found no alterations in the deeper structures.

The presence of an acute tension pneumothorax, alone or combined with pneumoperitoneum, was then studied. In the series of dogs, the air was injected into the abdominal cavity under sufficient pressure to cause distention of the abdominal wall. In this series the air did not leak out through the inguinal rings although the intraperitoneal pressure was high enough to cause urinary and fecal incontinence. Aside from the discomfort produced by the compression of the intra-abdominal

organs, no other symptoms were present. All these animals survived the shock of the experiment. In another series, an acute tension pneumothorax was produced by the injection of air into the chest through a needle. Depending on the compression of the lung produced by the pneumothorax, varying degrees of respiratory and circulatory embarrassment developed. In marked cases, asphyxia and death occurred, in more moderate cases, dyspnea occurred, and when the abdomen was opened from below, the diaphragm was seen to lose its tone and bulge downward into the abdomen. In this series a mediastinal, retroperitoneal and subcutaneous emphysema developed, but no air embolism was found. It appears, therefore, that an acute pneumothorax plays an etiologic part in the production of interstitial emphysema. Is it, then, the acute pneumothorax that kills these animals? In order to determine this point, we introduced compressed air into the lungs after we had previously inserted a small rubber catheter into each side of the chest to allow the escape of air from the pleural cavity. In this series we noted the characteristic subcutaneous mediastinal and retroperitoneal emphysema. These dogs, however, tolerated this change after a period of apnea lasting from fifteen to thirty seconds, so that the experiment could be continued for from two to three hours, when ordinarily a few blasts of compressed air into the lungs proved fatal. From these observations we may be justified in assuming that relief from acute pneumothorax keeps the animal alive in the presence of an interstitial emphysema.

The production of air embolism in these experiments has been fairly constant. In more than 80 per cent of the dogs that developed interstitial emphysema by the intratracheal injection of compressed air, we found large amounts of air in the cardiac chambers and in the general circulation. Air was present on the venous as well as on the arterial side, in the systemic as well as in the pulmonary circulation. To determine the effect of air embolism per se we injected air into the femoral vein. When from 200 to 300 cc of air was injected slowly over a period of from thirty to forty-five minutes, the dog remained alive. If, on the other hand, this amount was injected rapidly over a period of from four to five minutes, the dogs died promptly. Artificial respiration, cardiac massage or intracardiac injections of epinephrine failed to resuscitate the animal. When the heart was incised, we found the blood in a foamy state, and air bubbles of varying sizes were also present. Air could also be traced in the carotids, the aorta and the vena cava. It is possible, then, that with acute interstitial emphysema if the tension pneumothorax does not kill the animals the air embolism does. But how does the air get into the general circulation under these conditions? There are two possible routes. First, air may reach the circulation by means of a bronchovenous fistula. Such a fistula has been

produced experimentally by C M Van Allen<sup>5</sup> with a resultant air embolism. The second route is directly through the capillaries of the lung without any gross injury to the lung tissue. In a stereomicroscopic study of the lung in living animals, such as dogs, rabbits, alligators and frogs, we found that when the animal struggles or there is an increased intrapulmonic pressure microscopic bubbles of air are seen in the larger capillaries, and if such struggles persist these air bubbles become more and more numerous and extend to larger vessels. The frog is the best animal for such a study. We<sup>6</sup> have noted that with a slight struggle air finds its way into the larger vessels without any apparent change in the structure of the alveolar membrane. If the intra-alveolar pressure remains persistently high, all the larger capillaries become devoid of blood cells, and gradually the air bubbles reach the heart cavity. What probably happens is that the alveolar tension is increased to such a degree that more air passes into the capillaries than occurs under normal tension, but after the larger capillaries are reached the tension is again changed to normal with a resulting air embolism.

Another important fact which the studies on the frog revealed is that the alveolar membrane is made up of ridges and grooves, and the blood runs from the many celled capillary at the periphery over the surface of the alveolar membrane and divides into a massive delta so fine that air could easily find its way into these grooves without destruction of the membrane. When air embolism is produced, unless it is of a massive degree, the animal survives. The animal dies as a result of one of two causes. First, as the air reaches the heart chambers it is churned with the blood during the cardiac contraction and the blood becomes foamy. In this physical state of the blood, the contractions of the heart, instead of propelling the blood into the arteries, cause a greater emulsification. The animal dies of asphyxia and anoxemia. The second cause of death is air embolism of one of the vital centers in the medulla. When air finds its way there, it may remain long enough to cause anemia of any of these centers with possible death.

#### CONCLUSIONS

Interstitial emphysema is apparently a protective mechanism on the part of the body to keep air from parts where it may cause difficulty. A simple subcutaneous emphysema is harmless, and with a few small multiple incisions the air may be allowed to escape to the outside without causing any harm. If the condition causing the emphysema is persistent and as a result there is an acute pneumothorax and a pneumoperitoneum, the condition may be relieved if an outlet for the air is

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5 Van Allen, C M. Personal communication to the authors.

6 Joannides (footnote 3, second reference).

produced in the chest and abdominal cavities. No method has as yet been developed, however, to clear up an embolism of a massive type.

We have tried the combination of blood transfusion and venesection in order to replace the emulsified blood with normal blood, but without success. The condition of mild mediastinal emphysema and mild degree of an embolism is probably more common than is generally seen, because heretofore we have recognized only the extreme degrees of the condition. Our experiments lead us to believe that anything that produces an increased intrapulmonic pressure, such as a severe cough, child labor, lifting of heavy objects etc., probably causes a mild degree of mediastinal emphysema and air embolism, which as yet we have no way of recognizing clinically.



# A REVIEW OF UROLOGIC SURGERY

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*(Concluded from page 184)*

## URETER

*Tumor* —McCown<sup>30</sup> stated that primary carcinoma is rare, and that the paucity of symptoms makes diagnosis difficult. Early treatment is necessary to secure beneficial results, since tumors of this type result in widespread and rather early metastasis. He reported a case of tumor of the ureter. After various examinations, he concluded that a tumor of the ureter or of the kidney and ureter was present, and retroperitoneal nephrectomy was done through a lumbar incision. On liberation of the adhesions around the pelvis of the kidney, a mass was found in the ureter just below the pelvis, which was about 2 cm thick. The ureter was liberated and sectioned about 2 cm above the bladder. Evidence of extension was not found during the operation. Pathologic examination of the specimen revealed papillary carcinoma in the upper third of the ureter, without any evidence of metastasis or implantations along the ureter, as so frequently occurs in papillomatosis of the pelvis of the kidney.

Forty-three cases were reviewed, 21 of the patients were females and 22 were males. The right ureter was involved in 19 cases and the left ureter in 24. The neoplasm occurred in the upper part of the ureter in 5 cases, in the lower part of the ureter in 27 cases, and in the middle part of the ureter in 6 cases, it was diffuse in 1 case, near the center in 1 case, below the center in 1 case, multiple in 1 case, and it

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<sup>30</sup> McCown, P E Primary Carcinoma of the Ureter, J A M A 94 468 (Feb 15) 1930

involved the entire ureter in 1 case. The papillary type of carcinoma is the most common. The duration of symptoms from the cases reviewed was from five weeks to fourteen years. Hematuria was the most common symptom, it was noted in 31 cases. Tumor was reported as having been felt in 18 cases, in the final analysis hydronephrosis was reported in 32 cases. The clinical diagnosis of tumor of the ureter was made in 9 of the 43 cases. Nephro-ureterectomy had been performed in most cases. Involvement of the ureteral orifice required removal of a surrounding area of the wall of the bladder.

*Stones*—Ibrahim,<sup>11</sup> from his observation in Egypt, expressed the belief that most stones found in the ureter form in the pelvis of the kidney and pass into the ureter. Bilharziasis of the ureter is responsible for the majority of the stones primarily formed in the ureter. In most cases the cause is bilharzial ulceration, infection and surface concretions, in others it is infection of a dilated ureter above a bilharzial stricture. The latter type of stone is usually large and multiple. Most of the stones have a nucleus of oxalic or of uric acid, the remainder of the stone is composed of variable layers of oxalates, urates and phosphates. The variations depend on the chemical composition and reaction of the urine.

Ureteric colic is a constant symptom and is due to overdistention of the urinary tract above the level of the stone rather than to pressure of the stone or to spasm at the point of impaction. Frequency, pain and difficulty of urination occur with stones in the distal end of the ureter, but rarely accompany stones of the proximal end. In cases of intramural stones the picture may closely simulate that of vesical calculus. Hematuria, often only microscopic, is less common than in cases of renal calculus and is more severe during and after an attack of colic. The loin is always tender to deep pressure, as is the course of the ureter, especially at the level of the pelvic brim. The kidney may sometimes be felt enlarged. In a few cases the calculus may be felt on rectal or vaginal examination. Bilharziasis, when present, makes diagnosis more difficult. The urine is usually acid, showing erythrocytes and pus cells on microscopic examination. When complete obstruction occurs, pyuria disappears, although the condition of the patient becomes progressively more serious. When anuria caused by calculus occurs, the other kidney is usually absent or unhealthy.

Many small stones of the ureter pass naturally into the bladder, and slightly larger ones may pass under medical treatment. If the stone is more than 0.5 cm. in diameter, operation is indicated. There is less possibility of a rough or a spiculated stone passing naturally. When dilatation of the renal pelvis as a result of obstruction by stone occurs,

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31 Ibrahim, A. B. Stones of the Ureter, *Brit J Urol* 1:396 (Dec.) 1929

expectant treatment is contraindicated regardless of the nature of the stone. In cases associated with vesical calculus, Ibrahim operates on the bladder several weeks before he operates on the ureter. In cases associated with renal calculus of the same side and of a size small enough to make it possible for its later descent into the ureter, the kidney and ureter are operated on at the same time. If the renal stone is larger, it is removed by a second operation some time after the operation on the ureter. If the condition is bilateral, the better of the two sides is operated on first. In bilateral cases, if the stones are both in the distal end of the ureter, they may be removed advantageously at one operation through a median suprapubic incision. If bilharziasis is associated, the end-results are less satisfactory, but the decision concerning the operation is not affected. In operating on the upper part of the ureter, the ordinary lumbar incision is made because the ureter is not adherent to the peritoneum at this point. In operating on the lower part of the ureter, either the iliac or the median extraperitoneal approach may be used, the iliac being preferable. The incision is started near the anterior superior iliac spine and passes down, parallel to and 2.5 cm. above Poupart's ligament to about 2.5 cm. lateral to the pubic spine. The aponeurosis of the external oblique and the fibers of the internal oblique and transversus abdominis muscles are divided in the line of the incision in the skin. After the fascia transversalis is cut, the deep epigastric artery is divided between ligatures. The peritoneum is reflected to the bifurcation of the common iliac artery, where the ureter is looked for. It is usually retracted with the peritoneum but may be recognized by its feel and by the longitudinal arrangement of its vessels. Not more than 2.5 cm. of the ureter is dissected, care being taken not to denude the periureteric tissue which contains the blood supply of the adjoining segment of the ureter.

In 2 cases of calculous pyonephrosis with multiple small calculi in the kidney, the corresponding ureters being free, nephrectomy was performed. After operation the patients showed marked improvement from pain and intoxication from which they had been suffering. Later, definite signs and symptoms of severe cystitis developed. On cystoscopic examination the orifice of the ureter was found to be inflamed, immobile and patent, with pus exuding from it. The patients in these cases were successfully treated by excision of the remaining stump of the ureter by the suprapubic extraperitoneal route. A small stone was found in each stump. The supposition is that these stones must have slipped down the ureter from the kidney during manipulation for nephrectomy.

Over a period of three years, there was no mortality in 44 cases of stones of the ureter in which operation had been performed. At Kasr-el-Ainy Hospital, 2 deaths (4.8 per cent) occurred in 42 cases.

Bumpus and Thompson<sup>32</sup> summarized the data in 1 001 cases of stone in the ureter observed over a period of nine years. Pain originating in the renal area and radiating toward the bladder was noted in 634 (63.4 per cent) of the cases, but only rarely did it radiate to the inner side of the thigh or to the genitals. Pain in the lower right quadrant without radiation and with little suggestion of renal colic occurred in 138 cases. Because the symptoms simulated those of appendicitis the appendix was removed in 37 (26.8 per cent) of the cases, without relief from symptoms. Of the 1,001 cases, appendectomy had been performed in 226. Four hundred fifty-six patients noted marked frequency during attacks and 254 did not have urinary disturbances. Hematuria noticeable to the patient occurred in 300 cases and was demonstrated microscopically in 57 cases. Anuria was the most alarming symptom occurring in 27 cases, in 22 it was apparently reflex in type since obstruction was not demonstrable in the opposite ureter. The reflex anuria did not last more than twenty-four hours in any case. Anuria of longer duration is probably due to obstruction.

Stone could not be demonstrated by roentgenograms in 21 (2.1 per cent) of the cases. Without cystoscopic and other data the definite diagnosis of stone in the ureter cannot be expected in such a high percentage of cases because many of the shadows are indistinguishable from phleboliths. In 554 cases there was definite obstruction to ureteral catheterization. In many cases, this was passed easily with a catheter usually with little, if any, obstruction to the passage of urine.

In 146 cases the stone was passed following the manipulation incident to the first cystoscopic examination, whereas in 274 other cases manipulation was followed by success in 202 (74 per cent), in 65 of these, ureteral meatotomy was done as an aid to manipulation with scissors or with fulguration. In 63 cases surgical removal was necessary after the failure of manipulation. Two of these patients after their condition had been rendered critical, consented to operation but both died from sepsis. There were 252 cases in which stone was removed surgically from the lower third of the ureter and 228 in which the upper and middle thirds of the ureter were involved. In 49 cases the obstruction produced by stone in the lower part of the ureter had resulted in such extreme ureteral and renal injury that nephrectomy or nephro-ureterectomy was required. Excluding these 49 cases 60.7 per cent of all the stones in the lower part of the ureter were removed by manipulation. The operations performed in 529 cases were ureterolithotomy, 372; nephro-ureterectomy, 51; nephrectomy, 37; ureterectomy (nephrectomy elsewhere), 3, and combined operations 66.

<sup>32</sup> Bumpus, H. C., and Thompson, G. J. Stones in the Ureter. *Surg. Gynec. Obst.* 50:106 (Jan.) 1930.

Attempts to deliver stones by cystoscopic manipulation should not be carried to a point at which there is danger of suppurative pyelonephritis. Bumpus and Thompson are of the belief that in cases which show marked infection treatment should be by ureterolithotomy rather than by manipulation, the same holds true in cases with stones which are more than from 1.5 to 2 cm. in diameter and which are known to have been present for a considerable period.

Reaction following manipulation may be minimized if ureteral catheters are left in the ureter to insure drainage following the removal of the stone. The edema produced by the manipulation, together with the resulting ureteritis and periureteritis unless adequate drainage is insured, results in rapid ascending infection. When this has occurred, delay in operating to relieve the stasis and infection greatly increases the risk. In all the cases in this series in which operation was performed as soon as signs of renal infection appeared, the patients recovered. The 2 deaths from sepsis gave a mortality in the series of 0.2 per cent following catheter manipulation. There were 9 deaths following the surgical treatment of ureteral stones. The majority of these cases were complicated by the presence of renal stones and poor renal function, and the operation was done as a life-saving measure. The mortality in the entire series of 1,001 cases was 1.1 per cent.

[ED. NOTE.—These authors summarized from a large series of cases what would seem a proper evaluation of the various methods of treatment in cases of ureteral stones. The high incidence of previous appendectomy in the patients comprising this group is noteworthy and is a reflection on the failure of the average general surgeon to employ urologic methods of investigation in the usual case of so-called chronic appendicitis. If the roentgen rays and cystoscope were used more frequently, or even as a routine measure in such cases, many patients would be saved the ordeal and expense of an unnecessary laparotomy.]

We agree with the contention that when catheter manipulation is followed by sepsis or when impassable obstruction is encountered, then the indications for prompt surgical intervention are imminent.]

*Retained Stone After Nephrectomy*—Hunt<sup>33</sup> stated that subsequent operations on the ureter after removal of its adjacent kidney occur infrequently. Operations are seldom required on the ureter after nephrectomy has been performed for extensive infections of the kidney. Although infection of the ureter is often associated with infections of the kidney, patency of the ureter provides drainage of infectious material from the ureter with subsequent resolution of the process. If this were not true, ureterectomy would frequently be indicated after nephrectomy.

<sup>33</sup> Hunt, V. C. The Necessity for Operations on the Ureter, Including Ureterectomy, Subsequent to Nephrectomy, *J. Urol.* **23**: 43 (Jan.) 1930.

At the Mayo Clinic, during the last ten years, renal tuberculosis has provided the indication for nephrectomy in approximately 28 per cent of the major lesions of the kidney for which this operation has been necessary. In no instance in the series of approximately 574 cases in which nephrectomy was performed for renal tuberculosis during this period has subsequent ureterectomy been recorded. Experience has shown that the ureter, like the bladder, rarely remains infected after a tuberculous kidney has been removed. A search of the records at the Mayo Clinic revealed only one instance in which ureterectomy was necessary after nephrectomy for pyonephrosis. Noncalcareous infections of the ureter have been demonstrated to be rarely the cause of persistent pyuria subsequent to nephrectomy. The most common cause of pyuria from a ureter on the side on which the kidney has been removed is lithiasis, and if pyuria is present the indications are clear for ureterolithotomy or, preferably, ureterectomy.

*Foreign Bodies*—Stevens<sup>34</sup> stated that foreign bodies in the ureter, with the exception of stones, are rarely found. Entrance into the ureter may be directly from outside the body or from the kidney, intestines or bladder, the latter route being the most common. Contraction of the bladder or regurgitation may force or carry a foreign body from the bladder into the ureter. It may then travel upward as high as the pelvis of the kidney as a result of ureteral antiperistalsis and regurgitation. Catheters, bougies and other instruments should be carefully examined for imperfections before they are inserted into the ureter. Stevens reported two cases of broken instruments in the ureter, one in which a segment of a ureteral catheter, and the other in which a filiform tip was broken off into the ureter.

[ED NOTE—The dangers of broken off bits of catheters and bougies being retained in the renal pelvis or ureter was well emphasized by Stevens. The care that should be taken in selecting perfect instruments of this type for ureteral insertion and, what is more important, the need for routine observation of the catheter after removal, are obvious. When such an accident occurs the patient should be hospitalized and the urine carefully observed for the missing part. Further ureteral dilatation or even operation may become necessary if the retained particle fails to pass spontaneously.]

*Ureterocele*—O'Connor<sup>35</sup> stated that in order to avoid erroneous conclusions, ureterocele must be clearly distinguished from ureteral prolapse. In his series of 19 cases the ages varied from 19 to 60 years,

34 Stevens, W. E. Foreign Bodies in the Ureter. Report of Cases. California & West Med 32 104 (Feb) 1930

35 O'Connor, V. J. Ureterocele. A Clinical Study of Nineteen Cases. J Urol 23 33 (Jan) 1930

there were 12 women and 7 men. The left side was affected in 10 cases, the right in 4, and in 5 the condition was bilateral. General clinical observations support the premise that narrowing of the ostium is the primary factor in its production. The symptoms are variable and depend largely on the character and extent of the lesion in the upper part of the urinary tract. In treating the condition, transurethral or suprapubic coagulation of the cystic protrusion is most generally employed. In unusual cases, especially if the ureterocele contains calculi, suprapubic excision may be advisable. Nephrectomy should be reserved for cases in which injury to the corresponding kidney has been irreparable. When the condition is bilateral, coagulation of both sides should not be carried out simultaneously. In these instances dilatation of the ostium or its enlargement by slitting has been attempted before proceeding with unilateral coagulation. In addition, ureteral dilatation was done in all cases until a no. 12 French catheter could be inserted, this procedure was accompanied by appropriate treatment of the infection of the upper part of the urinary tract.

*Hydro-ureter* —Gruber,<sup>36</sup> in a series of experiments carried out on dogs, observed that excision of the ureterovesical valve, the vesical portion of the ureter, leads to the production of hydro-ureter. Removal of from two thirds to three fourths of the intravesical ureter does not render it incompetent to normal intravesical pressure changes. Progressive dilatation did not appear to change the activity of the ureter, both peristaltic and antiperistaltic contractions were observed. The maximal pressure of the ureter during contraction was 28 mm of mercury. The operation of meatotomy in human beings, performed through the operative cystoscope, is probably a safe procedure, as it appears unlikely that the entire valve will be cut during its performance. In the study of hydro-ureter in two pigs obstruction was not noted, and the valves were found to be edematous and incompetent.

*Indwelling Ureteral Catheters in Urinary Surgery* —Gutierrez<sup>37</sup> is of the belief that the indwelling ureteral catheter is the most valuable adjunct in urologic surgery, provided always that a correct diagnosis is made before establishing treatment. In acute clinical conditions, as in calculous anuria, if the indwelling catheter fails to relieve the symptoms, surgical intervention should not be delayed. One of the most common incidents in nephrolithiasis or ureterolithiasis is the calculous anuria or suppression of urine which tends toward the development of uronephrosis and fatal uremia. It has been proved that early operative

<sup>36</sup> Gruber, C. M. The Function of the Uretero-Vesical Valve and the Experimental Production of Hydroureters Without Obstruction, *J. Urol.* **23** 161 (Feb.) 1930.

<sup>37</sup> Gutierrez, Robert. The Value of Indwelling Ureteral Catheters in Urinary Surgery, *Surg. Gynec. Obst.* **50** 441 (Feb.) 1930.

intervention gives better results. Watson and Cunningham in an analysis of 205 cases of calculous anuria, in which a group of 110 patients was treated expectantly, reported deaths in 80 cases, a mortality of 72.7 per cent, and in another group of 95 cases, in which operation was performed, reported deaths in only 44 cases (46.3 per cent).

The diagnosis must be accurate and definitely clear because of the contraindications to the use of the indwelling ureteral catheter in extra-renal or intra-renal conditions when the pathologic process has become well advanced or does not communicate with the excretory apparatus, as in perinephritic abscess, cortical abscess of the kidney, or well advanced renal tuberculosis or hypernephroma. Surgical intervention is the most imperative hope of cure in the latter cases. The catheter to be used for diagnosis is preferably a no. 6 French, and for routine treatment a no. 7 or 8 French, of the type used in urography because it is more durable and flexible, and produces less discomfort. It is essential that the catheter secure drainage, relieve pain and correct infection. The fixed catheter should be irrigated at least three times daily with a mild antiseptic solution. In certain cases, when possible, two catheters in the same ureter and continuous irrigation may be definitely indicated. The catheter should be left fixed in place until the symptoms are completely relieved.

During operation the fixed ureteral catheter affords ready exposure of the ureter and facilitates any surgical procedure on the pedicle of the kidney. After operation it will serve to secure drainage and prompt healing of the wound, without leakage of urine or the formation of permanent fistula. It will also serve to divert the urine from the bladder, particularly in operations on vesicovaginal fistulas, thus permitting the bladder to heal without infection from the urine.

[ED. NOTE—The use of the indwelling catheter as a means of securing renal and ureteral drainage in various forms of infection and obstruction is well established. A few observers have offered a possible objection on the grounds that the catheter may produce pressure necrosis of the mucous and submucous tissues of the ureter with consequent sloughing. In rare instances death has been attributed to this source. Likewise it is well known that the presence of the catheter in certain acute cases seems to aggravate rather than to ameliorate the condition. Nevertheless, if the indwelling catheter can be kept freely draining, if it is well tolerated by the patient from the standpoint of pain, and if there are no evidences of exacerbation of symptoms, then the placing of such a drainage tube in the urinary tract is undoubtedly a great factor in reducing infection and in saving kidneys that otherwise might have to be removed.]



## BLADDER

*Surgery*—Keyes<sup>38</sup> stressed the importance of preventing pelvic cellulitis by prevesical section as a preliminary to suprapubic operation on the bladder. The mortality from preliminary suprapubic cystotomy has been estimated at 10 per cent. At Bellevue Hospital, over a period of six years, 102 suprapubic cystotomies were performed preliminary to prostatectomy, 32 of the patients died. In another series of 62 patients on whom a similar operation had been performed by various surgeons, 9 (14 per cent) died. Pelvic cellulitis was the predominant cause of death. By prevesical section, pelvic cellulitis may be prevented. As the first step of the procedure a catheter is tied into the urethra, and bilateral vasotomy and prevesical section are performed. The procedure is as follows. The prevesical space is opened through a median line incision and the distended bladder is recognized by palpation and by the veins visible beneath the posterior layer of the transversalis fascia. This fascia is split approximately in the median line and retracted laterally with the underlying veins. The muscle of the bladder is thus exposed from the upper edge of the pubes to the insertion of the urachus and laterally for about a finger's breadth from the median line. Three stout, plain catgut sutures are then introduced into the wall of the bladder, care being taken not to perforate the mucosa. One suture is inserted into the base of the urachus at the upper end of the denuded portion of the wall of the bladder, and by it the bladder is tied to the sheath of the rectus. Two other sutures are inserted into the wall, one on each side, at the edge of the denuded area, and are left long. A gauze pad, wet with 1:1,000 solution of acriflavine, is then placed against the denuded portion of the muscle of the bladder in the triangular space between the three sutures. The abdominal wall is closed in the usual manner above the point where the bladder is affixed to it. Below this point the muscle is pulled together by one or two sutures so as to prevent its spreading, and a corner of a gauze pad is pulled up through the incision in the skin, which is sutured around it. This drainage is necessary as much serum is thrown out into the wound. The bladder is not opened at this time. The urethral catheter supplies drainage and decompression.

After the operation, low decompression is employed. If no complications ensue, prostatectomy is performed on the third or fourth day. If the urethra will not tolerate the indwelling catheter, or if the patient is delirious and pulls the catheter out, or if his condition is such as to require prolonged drainage before the prostate gland is removed.

38 Keyes, E. L. Pelvic Cellulitis Following Suprapubic Cystotomy and Its Prevention by Prevesical Section, *J. Urol.* **23** 119 (Jan.) 1930.

the bladder may be drained suprapubically at any time after twenty-four hours have elapsed from the prevesical section, with the assurance that pelvic cellulitis will not follow

Suprapubic prostatectomy with the use of prevesical section has been performed on 29 patients without mortality. Such preliminary section is desirable not only because it eliminates postoperative mortality but also because it does away with the interval of waiting for the patient to recover from pelvic cellulitis before prostatectomy can be done

Suprapubic lithotomy for a large stone is attended by high mortality, which has been attributed to the poor renal function shown by these patients. Preliminary treatment does not affect the renal function nor the infection of the bladder, death occurs from pelvic cellulitis. Transperitoneal cystotomy has been suggested as the safest route of approach because it eliminates the risk of such cellulitis. Keyes has performed this transperitoneal operation successfully on several patients who would doubtless have not survived the suprapubic section

*Tumors*—Kidd<sup>39</sup> stated that the many attempts to perform complete cystectomy for carcinoma of the base of the bladder have not been encouraging because of the high immediate mortality due to shock, sepsis and chronic uremia. The condition of the few patients who have survived the operation has not always been satisfactory. The operation has been most successful when the ureters were transplanted to the skin and the bladder was removed at a second operation. The operation has been attended by the highest mortality when attempts have been made to divert the ureters into the rectum and remove the bladder either at the same operation, which entails considerable shock, or at a second operation, which entails increased difficulties from adhesions caused by the first operation. Kidd performs cystectomy for carcinoma of the base of the bladder with resection of both ureters, and yet leaves the patient with a functioning bladder. In some of these cases there is usually present on one lateral wall and toward the apex of the bladder a healthy portion of mucous membrane. This is sacrificed in the usual operations for total cystectomy, but by Kidd's technic it is used as a graft or plastic flap to make a new bladder, into which the resected ureters can be made to empty their effluents. This operation has been carried out in two cases with success and it is hoped that it may eliminate the dangers and disadvantages of the older methods of cystectomy

In one case, at operation, the growth was cut away quickly, and no attention was given to bleeding points, which were dealt with at a later

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39 Kidd, Frank. Cystectomy for Carcinoma of the Bladder-base with Restoration of Bladder Function, *Brit J Urol* 1: 380 (Dec.) 1929

stage There remained a healthy portion of the right lateral and superior wall of the bladder supplied with blood by the intact right vascular pedicle of the bladder and still attached to the right lateral wall of the pelvis, and the two ureters cut across and lying loose on the pelvic floor The bladder was reconstructed as follows Into each ureter was inserted a special implantation catheter devised for use in resection and transplantation of the ureters into either the bladder or bowel or onto the skin Two ligatures of catgut were then tied tightly around the ureter By this device the ureteral catheters were fixed firmly by the ligatures into the mouths of the ureters, yet the urine was in no way prevented by the ligatures from escaping freely from the mouths of the catheters The ligatures sealed the lymphatics of the ureters, thus closing the path of ascending infection during the process of healing The ligatures were left long and used at a later stage for fixing the ureters where it is desired to do so The two ureteral catheters were pulled out through the urethra and left emerging from the penis The two ureters were left high and dry running across the floor of the pelvis, and their ends were approximated to the severed posterior end of the urethra by means of the catgut ligatures that fixed them to the ureteral catheters With the help of several catgut stitches the front portion of the right lateral wall of the bladder was drawn inward beneath the two ureters and attached to the tissues on the floor of the pelvis to the left of the rectum It was then possible to draw the hinder or upper portion of the flap of mucous membrane of the bladder underneath the ureters to the left side of the pelvis and bring it around on the left side and stitch it loosely by two catgut stitches to the upper anterior portion of the right lateral wall of the bladder In this way the ureters and the tube were more or less surrounded by a plastic flap of mucous membrane The operation was performed in one hour and fifty minutes

The patient recovered from the shock of the operation He had a certain amount of fever from the seventh to the thirteenth day caused by stitch abscesses in the upper portion of the wound, during the remainder of the illness there was no increase in temperature The ureteral catheters drained clear urine, free from pus, and were taken out on the nineteenth day A suprapubic tube could be inserted through the suprapubic sinus into the new bladder and could be left in place Lavage was carried out through the urethral catheter and suprapubic tube for a week On the twenty-ninth day the tube and catheter were removed, and the bladder was washed out daily with silver nitrate On the thirty-third day the patient began to urinate naturally and easily On the forty-third day, the suprapubic wound was healed and the catheter was removed From then on the patient passed urine naturally and easily through the penis He had complete continence and could

retain urine for two hours as much as 120 cc passed at one time with a good stream. Five months later he was able to retain urine from two to three hours there was a good stream, no incontinence and no hematuria. Only a trace of pus was found in the urine. There was no thickening of the base of the bladder to be felt by rectal examination.

MacKenzie<sup>40</sup> reviewed from the literature 21 cases of small round cell sarcoma of the bladder to which he added a case of his own, making a total of 22. A marked difference in the age incidence was noted in the two sexes. In 9 of 20 cases in which the site of the tumor was mentioned it was situated around the trigone on the base of the bladder and around the vesical neck. Six were on the lateral walls, extending down to and in some cases involving, a ureteral orifice, and 4 were on the roof or posterior wall of the bladder. In 7 of the 22 cases, operative treatment had not been given, or it was not stated. In 5 cases palliative cystotomy (3 suprapubic and 2 perineal), and in 1 case palliative ureterostomy was performed, in 1 case in which diagnosis was made at cystoscopic examination, a specimen was removed for examination. In 1 case the tumor was removed through the vagina and radium was applied. In the other 7 cases a radical attempt was made to remove the growth. The results in all cases were extremely poor. Only 1 patient was cured. This patient is alive and well nine years later. In many of the cases, death followed immediately or a few days after the operation. Eight patients died within three months of operation. Two of the patients not operated on lived two and seven years, respectively.

Beer<sup>41</sup> reported 8 cases of total cystectomy and partial prostatectomy for infiltrating carcinoma of the neck of the bladder, with only 1 death (12.5 per cent). In 7 cases in which the operation was done by the extraperitoneal procedure with implantation of the ureter into the skin, there was no mortality. The patient who did not survive died ten days after the operation with infection of the left kidney due to implantation of the ureters into the sigmoid. Of the 7 patients who survived, 1 patient lived five years, 1 lived nine months, 1 with leiomyosarcoma lived two months and the remaining 4 patients are still alive four years, one and a half years, seven months, and six months respectively, after operation. Since all of the patients of this series were males, Beer's technic is applicable to that sex.

Beer concluded that the mortality of extraperitoneal removal of the bladder with the adjacent prostate gland is not prohibitive and the operation can be done in one step with implantation of the ureters into the skin without undue risk to the function of the kidney. Even

40 MacKenzie, D. W. Small Round-cell Sarcoma of the Bladder with Review of the Literature, *Brit J Urol* **1** 359 (Dec) 1929.

41 Beer, Edwin. Total Cystectomy and Partial Prostatectomy for Infiltrating Carcinoma of the Neck of the Bladder. *Ann Surg* **90** 864 (Nov) 1929.

though the patients are obliged to wear an apparatus for the collection of urine, they are relieved of their original painful condition, are rendered fairly comfortable and are well able to get about

[ED NOTE—Total cystectomy would seem to offer the best opportunity for cure in cases of widespread carcinoma of the bladder which are irresectable with the bladder in situ. C. H. Mayo and Hunt, stimulated by the work of Coffey, have recently been perfecting the technic of ureteral transplantation into the sigmoid. Their results have been encouraging. If this method of shunting the urinary stream proves practicable, it would seem to offer a better mode of disposing of the output of urine than that of transplanting the ureters into the skin, as practiced by Beer. Regardless of the method of choice for subsequent drainage of the urine, the contention that total radical removal of the bladder and prostate gland for widespread malignancy will be followed by a higher percentage of cures seems well established in the light of early experience with the method.]

Young<sup>42</sup> stated that in radical resection of infiltrating tumors the best results have been obtained at the vertex and adjacent portions of the bladder. In such cases, if the peritoneum overlies the site of the tumor, it has been his practice to open the peritoneal cavity and carry out resection at a point distant from the growth. In this way a sufficiently wide area of peritoneum is removed in one piece with the wall of the bladder. In cases of tumor of the posterior wall of the bladder not involving the vertex, the intraperitoneal operation is often not satisfactory, because of the difficulty of reaching the peritoneum in the deepest part of Douglas' pouch and the bladder below that point.

Young recently employed a new procedure in which the tumor of the posterior wall of the bladder with its peritoneal coat is resected entirely through an intravesical operation. The technic is as follows. A long median-like incision is made from the pubes almost to the umbilicus and recti muscles separated in the median line and widely retracted. Incision is made into the bladder in the median line rather close to the prostate gland, and carefully enlarged above and below and widely retracted until a good view of the interior of the bladder is obtained. The ureters are then located and their proximity to the tumor and its infiltrated base determined. The area of removal is demarcated by placing eight Allis clamps in cardinal positions around the tumor, and at a distance of at least 1.5 to 2 cm. from its outermost invasion. Making traction on the upper clamp, a transverse incision is made with the scalpel through the mucosa, submucosa and muscle of the bladder until

<sup>42</sup> Young, H. H. Treatment of Certain Vesical Neoplasms by Intravesical Resection of the Entire Bladder Wall with the Peritoneal Coat, *J. Urol.* **23**: 269 (Feb.) 1930.

the outer surface of the peritoneum is recognized. This is then picked up with two Allis clamps and divided transversely with a knife. The resection is carried out by scissors on each side, going well away from the mass and external to the Allis clamps. When the lower portion to be resected is reached, if it is found to extend beyond Douglas' pouch, the peritoneum is divided transversely at the depths of the culdesac, and resection continued on downward and across the lowermost area selected for resection. Thus the mass, with its peritoneal covering is removed in one piece.

By such exposure it is possible to include retrovesical and peri-ureteral structures in a more radical manner than when complete mobilization of the posterior and lateral walls of the bladder and the delivery of the bladder externally has been carried out.

Schuller<sup>43</sup> stated that the efficacy of radiotherapy in urology is not standardized. In his experience, 3 papillomas of the bladder reacted favorably to deep applications, and in 1 case, an apparently recurrent papillary carcinoma of the trigone disappeared after the insertion of radium needles, followed by the use of deep applications. He concluded that papillomas of the bladder are amenable to roentgen treatment, and that such treatment should be tried in cases in which resection is impossible and before ureteral transplantation to the bowel is undertaken.

*Extravesical Tumors*—Hochloff<sup>44</sup> reviewed 106 cases of carcinoma of the cervix in which he had made cystoscopic examinations. These were divided into three groups. Group 1 consisted of cases in which the mucous membrane was normal or there was hyperemia of the trigone, folding of the walls and tiny hemorrhages in the mucous membrane. Group 2 consisted of cases in which the cystoscopic picture was bullous edema of the trigonal mucous membrane and other areas of the bladder. The ureteral orifices were usually raised on a swollen background and their contour was changed. Group 3 consisted of cases of diffuse, square-shaped areas of edema of the mucous membrane, especially over the area of the trigone, making it almost impossible to find the ureteral orifices. In other cases the orifices were somewhat tilted and surrounded by an edematous hyperemic wall. Dilatation of the blood vessels in the mucous membrane were characteristic of the cases in groups 2 and 3.

In group 1 no difficulties were found at operation in the parametral tissues. In group 2 difficulty not infrequently arose in freeing the ureter. The uterus was only slightly movable and there was infiltration of the adjacent connective tissues. In group 3 usually diffuse spreading of the carcinoma into the wall of the bladder was found.

43 Schuller, Hugo. Zur Radium- und Röntgentherapie in der Urologie. *Ztschr f urol Chir* 27 374 (July) 1929.

44 Hochloff, A. W. Zur Wertung der Chromocystoskopie beim Carcinoma colli uteri, *Ztschr f urol Chir* 27 438 (July) 1929.

*Rupture*—Campbell<sup>45</sup> stated that rupture of the bladder occurs rarely but the condition is diagnosed with difficulty and the mortality, therefore, is high. In many instances the diagnosis is made only at operation or at necropsy. Of 55 patients treated in Bellevue Hospital, 35 (63.6 per cent) died, a mortality rate which is in accord with other observations. More than 90 per cent of the ruptures occur in males. Of the patients suffering from intraperitoneal involvement 26 (73.5 per cent) died, only 9 (42.9 per cent) of those with extraperitoneal involvement died. The operative mortality of the group with extraperitoneal involvement was 40 per cent, of the group with intraperitoneal involvement, 68 per cent. A summary of reports of cases from the literature indicated that from 60 to 80 per cent of patients die even under the most favorable surgical conditions.

Distention and alcoholism and other forms of mental irresponsibility are important predisposing causes of vesical rupture. In 19 cases, the ruptures occurred during acute alcoholism. In 9 cases (16 per cent), the rupture was due to injury by automobiles, 8 of these patients were pedestrians. In 11 cases, the rupture followed a fall. Apparently the distance fallen is comparatively unimportant, 1 patient who died fell only 4 feet. Another, who lived, fell a distance of eight floors. In 12 cases, the rupture resulted from crushing injuries. Associated pelvic fracture occurred in 20 cases. In 166 cases of fracture of the pelvis occurring over a period of nine years, there was vesical rupture also in 25 (15 per cent). In 3 others, rupture of the posterior urethra had occurred.

In most cases of rupture of the bladder, shock follows the injury, one fourth of the 55 patients were in shock, were comatose, or were moribund. The general appearance and physical condition of many of these patients strongly indicated internal hemorrhage. Involvement of the urinary tract is suggested by local tenderness of the bladder, dysuria, hematuria or absolute inability to urinate. If intraperitoneal rupture has occurred, early symptoms of peritonitis may be present. Abdominal tenderness and rigidity appear first, then nausea and vomiting. Extraperitoneal rupture was found in 21 cases, whereas intraperitoneal rupture with free urine in the abdominal cavity was observed in 34. Marked abdominal rigidity was present in 22 cases, and unusual distention was seen in 31.

The emergency condition of most of these patients precludes protracted diagnostic procedures. Catheterization is the most commonly employed and one of the most inaccurate diagnostic tests. Often there is no return of urine, or a small amount of blood may be withdrawn. At

<sup>45</sup> Campbell, M. F. Rupture of the Bladder. A Clinical Study of Fifty-Five Cases, *Surg. Gynec. Obst.* 49:540 (Oct.) 1929.

times a large amount of urine will flow, more than the apparently undistended bladder would indicate, which signifies drainage of an abdominal cavity filled with urine. The injection of a measured amount of fluid and the estimation of its return should always be attempted, although this method is not absolutely accurate. If the catheter has penetrated an abdominal pool of urine, a larger quantity of fluid will be withdrawn. Diagnostically, this constitutes the most significant of any of these observations. Catheterization, although used in 41 cases, was of diagnostic value in only 13. In almost all cases, urine containing blood was withdrawn. When physical conditions permit, cystoscopic examination is the most accurate method of diagnosis.

Operation should be performed as soon as the diagnosis of ruptured bladder is made. Anesthesia by nitrous oxide and oxygen or by ethylene is preferable in most instances. Spinal anesthesia is contraindicated in the presence of marked vascular depression with low blood pressure. In most cases intraperitoneal exploration is indicated. Operative speed is essential. If no evidence of urine within the peritoneum is found the peritoneum is closed and the interior of the bladder is investigated. If peritoneal involvement is present, such fluid as is readily obtained is aspirated and ample drains are left in place. Flushing out the abdominal cavity, with solution of sodium chloride or medicated solutions, is inadvisable as it wastes time and disseminates infection. The vesicoperitoneal tear is hastily closed by a minimum of sutures firmly grasping the musculature of the bladder. It is unnecessary to attempt to suture the layer of muscles of the bladder. Liberal suprapubic drainage of the bladder is of prime importance. Campbell uses a three-fourth inch tube for this purpose. With free drainage, bleeding and extravasation will stop at once and smaller unsutured bladder wounds will heal readily. Penetrating wounds caused by the bony spicules of pelvic fracture are rarely large enough to require suture. Bony spicules, stones or other foreign bodies in the bladder should be removed while it is open.

Of 20 patients who were operated on and survived, 5 were able to leave the hospital in less than three weeks, 6 left in from three to six weeks, 5, in from six to twelve weeks, and 4 remained in the hospital more than three months. The longest stay was six months. Of the 35 patients who died (10 of whom were not operated on), 2 lived less than ten minutes after admission to hospital. Ten died within the first twenty-four hours, 14 died within three days, and all but 4 died in less than one week. One lived eight months. Campbell concluded that if the patient survives the first week, a fair prognosis is likely. In all cases a grave prognosis is warranted during the first week.

[ED. NOTE.—Since rupture of the bladder is a condition which the average urologist encounters infrequently, this report from a clinic in which a large volume of work is done on patients suffering from trauma



is of more than passing interest Campbell emphasized mental incompetence, distention of the bladder and a variable type of trauma as the factors usually associated in producing the condition The urgent need for immediate diagnosis as well as the difficulties encountered in making oneself certain of the existence of the lesion are well outlined The necessity for prompt surgical intervention in the intraperitoneal types of rupture and the early avoidance of operation in vesicorectal and vesicovaginal ruptures are in keeping with good judgment according to Campbell's experience ]

*Submucous Cystitis*—Donohue <sup>46</sup> stated that there are two separate and distinct etiologic factors concerned in the production of submucous cystitis extension from long-continued or recurring infections of the mucosa of the bladder, and dissemination from inflammatory foci in structures outside the urinary tract Lesions representing extensions from infections within the bladder are usually extensive, the condition of contracted bladder being the common sequel When submucous cystitis is the result of embolic hematogenous bacterial invasion, the lesions are usually well localized, the remainder of the bladder retaining its elasticity and tonus Beneficial results cannot be assured in treating extensive lesions of either type of submucous cystitis Lesions which are not extensive and well localized regularly respond to appropriate treatment

[ED NOTE—Donohue differentiates submucous cystitis as due to long-continued or recurring infection of the bladder or due to focal infection, according to the concept of Hunner Whether the former should be included as true submucous cystitis was challenged during the discussion of this paper The main point stressed by Donohue and with which urologists of experience are in accord is the deplorable inadequacy of present methods of treatment, such as resection, fulguration, and overdistention No one suffers more or can be offered less than a patient afflicted with this disease ]

*Perforation*—Wilhelm <sup>47</sup> stated that perforation of the bladder during cystoscopic examination occurs more frequently than the few reports in the literature of a similar condition would indicate Cystoscopic examination should not be attempted in the case of unruly and uncooperative patients, and it is hazardous to perform it under gas and oxygen anesthesia The introduction of fluids or gases into a perforated bladder for diagnostic purposes is a dangerous and unreliable procedure Diagnosis of this condition should be made by means of the clinical history The differential diagnosis of intraperitoneal and extraperitoneal perfora-

46 Donohue, P F Submucous Cystitis, J Urol **22** 465 (Nov) 1929

47 Wilhelm, S F Perforation of the Bladder During Cystoscopic Examination, J Urol **22** 555 (Nov) 1929

tion is difficult, if not impossible, and in cases of doubt exploratory laparotomy should be performed. When the perforation is into the rectum or vagina, the treatment is nonoperative. Immediate surgical intervention is indicated in all other cases of perforation of the bladder.

#### PROSTATE

*Hypertrophy*—Takeichi<sup>48</sup> found that the conservative use of radium in the treatment of prostatic hypertrophy affords good results. Improvement in urination and a definite receding in the prostatic swelling were demonstrated. Complications were not observed during the course of the healing processes.

*Carcinoma*—From the reports of the Necker Clinic, Dossot<sup>49</sup> studied 154 cases of carcinoma of the prostate gland, including 82 histologic examinations of the operative specimen and 63 reports on necropsies. Prostatic adenoma plays an important part in the pathogenesis of numerous carcinomas, in 11.6 per cent of cases malignant transformation was noted. Two types of prostatic carcinoma should be distinguished: urethroprostatic adenocarcinoma which develops from the adenomatous glands of the prostatic urethra, and true carcinoma of the prostate gland which develops from the gland itself. Among 134 cases of primary carcinoma there were 61 urethroprostatic adenocarcinomas, 17 adenomas suspected of degeneration, 46 true carcinomas of the prostate gland, and 6 probable true carcinomas with adenoma. In 13 cases the nature of the carcinoma was not specified. Carcinoma and adenoma were found associated in 58.7 per cent of cases.

Geraghty, in a series of 450 prostatic carcinomas, noted its association with hypertrophy in 75 per cent of cases, but it is his belief that the two conditions are absolutely independent. Shaw, in more than 1,000 operative specimens of carcinoma of the prostate gland examined at Johns Hopkins Hospital, found only 2 cases in which the carcinoma developed in the middle of the hypertrophied lobule.

Extension in carcinoma of the prostate gland occurs early, and before it can be recognized clinically the carcinoma has extended far beyond the limits of the gland and has invaded the pelvic and abdominal lymph nodes.

Prostatectomy and irradiation have given only mediocre results, and cures of more than three years are unusual. True cures can only be obtained in cases in which operation is performed with a diagnosis of adenoma and in which histologic examination shows the existence of

48 Takeichi, T. *Erfahrungen mit der Radiumtherapie bei Prostatihypertrophie*, Japan Ztschr f Dermat u Urol **29** 31 (Jan) 1929.

49 Dossot, Raymond. *Cancer of the Prostate. Its Origin and Extension*. J Urol **23** 217 (Feb) 1930.

carcinoma When carcinoma has progressed to a recognizable stage, it is generally extensive With the present state of knowledge of carcinoma of the prostate gland it is advisable to limit efforts to palliative treatment, such as the passage of sounds and cystostomy

#### TESTIS AND EPIDIDYMIS

*Seminal Vesiculectomy*—Gutierrez<sup>50</sup> reviewed the results of operation on 100 mentally defective patients for definite pathologic lesions of the seminal vesicles The operations had been performed six years previously In 98 cases, bilateral seminal vesiculectomy was performed and in the other 2, vesiculotomy and prostatotomy Ether and gas were used for anesthesia All the patients of this series recovered uneventfully both from the immediate traumatism of the operation and from the general condition Perineal or rectal fistula has not been seen, nor has epididymitis or any other common urologic complication occurred The membranous urethra, although exposed during the operation, was not opened in any instance Deaths did not result from the operation, although there were 8 deaths due to different causes, occurring at an average time of two years and three months after operation On reexamination of the patients, the ampulla was found to be patent and easily palpable by rectum in more than 21 per cent of the cases Sexual function was apparently unchanged in most instances Of the specimens removed at operation, 38 per cent showed infection or positive culture Histologic sections revealed the presence of inflammatory changes of chronic vesiculitis in many cases Forty-eight per cent of the patients were dismissed from observation or were definitely improved; 52 per cent remained mentally unimproved The elimination of foci of infection is especially worthy of consideration in dealing with mentally defective patients

*Scrotal Gangrene*—Gibson<sup>51</sup> reported a case of idiopathic gangrene of the scrotum The onset was sudden, without apparent cause, and was accompanied by extreme toxemia The gangrene spread rapidly from the scrotum along superficial planes to the axilla The patient died four days after onset, presenting the typical picture of a severe case of gas gangrene Necropsy did not reveal a cause of the disease

Two hundred six cases were reviewed from the literature The mortality of the group was 26.7 per cent The three main characteristics of the symptoms of the disease were the sudden appearance of the phe-

50 Gutierrez, Robert Later Results of Surgery of the Seminal Vesicles Report of One Hundred Consecutive Seminal Vesiculectomies, J A M A **93** 1944 (Dec 21) 1929

51 Gibson T E Idiopathic Gangrene of the Scrotum with Report of a Case and Review of the Literature, J Urol **23** 125 (Jan) 1930

nomena in the midst of apparent health, the rapid evolution of mortification, and the apparent total absence of any of the usual causes of gangrene. The process spreads frequently upward from the scrotum along superficial fascial planes and may extend to the axilla. In many cases no external lesion or disease of the genito-urinary organs can be discovered to explain the origin of the infection. Two theories may be considered as to its inception: a slight external scratch or abrasion unknown to the patient at the time serves as a portal of entry for the infecting organisms, or a minute lesion, such as an infected node in the urethra, is the starting point of the infection. The disease is subject to considerable variation in virulence, patients die as early as thirty-six hours and as late as thirty-three days after onset. Gangrene usually appears about three days from the onset of symptoms.

Treatment in general should be similar to that used in cases of extravasation of urine, that is, incision and disinfection. Because of the undoubted anaerobic nature of some if not all, infections of the external genitals accompanied by gangrene, the use of antigangrenous serum or anaerobic antitoxin should be given a trial. Even though the whole scrotum sloughs away, satisfactory regeneration will take place.

*Dislocation of the Testis*—Alyea<sup>52</sup> stated that cryptorchidism occurs in from 0.1 to 0.2 per cent of all young adults. Aberrant migrations of the testis are less common than cryptorchidism. The congenital perineal testis is the most common type, more than 100 cases have been reported.

Twenty-three original cases of traumatic dislocation of the testis were found to be reported in the literature, to which Alyea added 2 cases. The resultant position of the dislocated testis is dependent on anatomic abnormalities, on obstruction to dislocation in particular directions and on the direction and force of the blow. In most cases the etiologic factor was the passage of a wheel over the genital region, this was followed by severe shock, local pain, and nausea and vomiting. Diagnosis was usually simple after the disappearance of traumatic swelling. Treatment was satisfactory, reduction without open operation was accomplished in three cases, and open reduction was performed in 16 cases.

Herniation or compound dislocation of the testis would seem to be a condition likely to occur in many industrial accidents, but only 3 cases are reported. One of the 2 cases presented by Alyea is of this type. Prognosis in all cases is excellent.

*Tuberculosis*—Wang<sup>53</sup> stated that it is difficult to evaluate the results of treatment with tuberculin, particularly when it is part of a

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<sup>52</sup> Alyea, E. P. Dislocation of the Testis, *Surg Gynec Obst* 49:600 (Nov.) 1929.

<sup>53</sup> Wang, S. L. Tuberculin Therapy in Urologic Tuberculosis, *J. A. M. A.* 94:235 (Jan. 25) 1930.

general course of treatment. Other factors, such as the natural tendency of most patients to improve after operation and the periods of latency of symptoms which occur with both inoperable and postoperative cases of tuberculosis of the genito-urinary tract must also be considered. In a series of 55 cases of inoperable, postoperative and preoperative tuberculosis in which lesions were localized in the genito-urinary tract, an effort was made to ascertain whether the patients were benefited by tuberculin treatment, according to the plan that has been carried out. Of the 55 patients, the condition of 39 was improved, of 8 it seemed stationary, and of 7 it was retrograde. One patient died. Besides the tuberculin treatment, these patients received mercury-vapor-quartz light and other treatment. It could not be determined which of these procedures was the most favorable, but tuberculin appeared to have been helpful. In the three years during which the tuberculin had been administered it was evident that there were few, if any, standards for its use in this form of tuberculosis. Tuberculin is not a cure for tuberculosis of the genito-urinary tract, as demonstrated by the time and extent of its usage, but there is considerable evidence that it aids in building up the general health of the patients. In the treatment of patients with inoperable conditions following operation, it has seemed to be a helpful factor.

#### PENIS

*Leukoplakia*—Fukai<sup>54</sup> reported on the rare occurrence of leukoplakia or leukokeratosis of the penis. He found reports on only 43 cases in the literature since the first case reported by Perrin in 1892. Recently he had observed 6 such cases. Usually the lesions occur in congenital phimosis. The process begins as a small wartlike structure, but later becomes diffuse and covers the glans and the inner lining of the prepuce. One case progressed to the formation of carcinoma of the urethra.

#### URETHRA

*Bleeding*—Ghingar<sup>55</sup> differentiated spontaneous hemorrhage from the meatus. If spontaneous bleeding is from the external meatus, it is definitely an anterior urethral hemorrhage. Hemorrhage during micturition is a form of significant hematuria. It is important to determine whether the blood originates from the urethra and from which specific portion. Initial hematuria signifies urethral bleeding without definite localization, terminal hematuria means bleeding above the external sphincter, although, under some conditions, bleeding from the

<sup>54</sup> Fukai, A. Leukokeratosis glandis et praeputii penis, *Acta dermat* **11** 528 (June) 1928.

<sup>55</sup> Ghingar, A. Pathologie und Therapie der Harnrohrenblutungen, *Ztschr f Urol* **23** 81, 1929.

anterior urethra may simulate terminal bleeding, whereas total hematuria leaves all possibilities open. For topographic diagnosis endoscopic, urethroscopic and cystoscopic examinations are necessary. Ejaculatory bleeding is one of the causes of hemospermia. Experience has shown that bleeding associated with defecation occurs in the posterior part of the urethra.

#### URINARY ANTISEPTICS

Kaufman<sup>56</sup> stated that in the treatment of infection of the urinary tract the importance of drainage should be recognized. Water is essential, with certain physiologic aids, in combating pyrexia, toxemia and renal failure.

The purpose of urinary antiseptics is clearly established on both scientific and clinical grounds in the treatment of acute and chronic infections. Clinical cure is obtained in acute pyelonephritis and cystitis by alternate alkalinization and treatment by acid hexamethylenamine. This treatment does not usually bring about actual sterilization of the urinary tract. In chronic urinary infections, including those without serious organic lesions and those in which infection persists after operative removal of organic lesions, urinary antiseptics are promising aids. No single antiseptic has been found which is universal.

Hexamethylenamine is of definite value, particularly as a prophylactic against infection in instrumentation of the bladder, in the simpler forms of acute infections, and in general routine postoperative care. Kaufman expressed the belief that acidifiers should always be used and found that a safe combination was phenyl salicylate, methenamine and sodium benzoate. Intravenous therapy offers an opportunity for prompt concentration of the antiseptic. Mercurochrome-220 soluble, if used intravenously in effective dosage, produces severe reactions. For local use, mercurochrome is the most effective for actual sterilization, especially in operative cases. For general use, acriflavine was observed to be better tolerated although apparently less efficient. It is Kaufman's belief that mercurochrome is superior to acriflavine in the treatment of staphylococcus infections, as well as in chronic infections from colon bacillus. Silver nitrate is invaluable in actively stimulating repair, a factor which may materially assist in sterilization of the urinary tract. Boric acid is a passive antiseptic, indispensable for cleansing, it does not irritate and is clinically satisfactory.

Thomas and Wang<sup>57</sup> studied six compounds, none of which could be considered as an ideal urinary antiseptic. When mercurochrome is

<sup>56</sup> Kaufman, L. R. A Clinical Consideration of Urinary Antiseptics, *J Urol* **22** 163 (Aug.) 1929.

<sup>57</sup> Thomas, B. A., and Wang, I. K. Studies on the Comparative Clinical Values of Various So-Called Urinary Antiseptics, *J Urol* **22** 22 (July) 1929.

given in dosage of 300 mg three times daily by mouth in salol-coated pills "about 30 per cent of the urine from the bladder will become antiseptic" Hexylresorcinol administered in 25 per cent olive oil in dosage of 0.6 Gm three times a day has the same disadvantages as mercurochrome, and the antiseptic value in the urine is much less. Fifteen grains (0.97 Gm) of hexamethylenamine three times daily frequently caused indigestion, and the bactericidal effect on the urine was not certain. The germicidal strength of methylene blue was higher than expected, but the dye did not usually produce sufficient concentration in the urine to be of antiseptic value. Pyridium administered in dosage of 0.2 Gm three times daily by mouth proved to be a weak antiseptic, and its action against the colon bacillus was practically valueless. Salol has no standing as an urinary antiseptic, since the phenol content excreted in the urine never reaches a germicidal strength. It apparently rendered the urine bland and less irritating to an inflamed urinary tract, thereby giving a certain amount of comfort to patients.

[ED NOTE—One must conclude from this and from other recent studies of the comparative value of urinary antiseptics that they are still far from ideal. No drug is as yet available which will render the urine strictly bactericidal *in vivo*. We are forced to the conclusion that in chronic infections of the urinary tract we must consistently rely on the methods of instrumental drainage and lavage as a means of therapeutic attack.]

#### UROLOGIC CONDITION IN EARLY LIFE

Stevens<sup>58</sup> reviewed the histories of the last 9,115 patients admitted to the pediatric department of Stanford University Hospital and found that 205 suffered from one or more pathologic conditions of the urinary tract. One hundred six of the 205 patients were males and 99 females. Pyelitis occurred in 74 cases, nephritis in 35, phimosis in 28, undescended testis in 13, cystitis in 11, enuresis in 10, pyonephrosis in 6, urethral stricture in 5, nephrolithiasis in 3, redundant prepuce in 3, hydroceles in 4, and tuberculosis of the kidney in 2. In infancy and childhood pyelitis is the most common pathologic condition of the urinary tract. It occurred in almost a third of the patients and was found about four and a half times as often in females as in males.

Urinary calculi are frequently observed during infancy and childhood. They are found more often in the lower part of the urinary tract, although they usually originate in the kidney. In 2,313 reported cases of pathologic conditions of the urinary tract, renal calculi were found in 11 cases, ureteral calculi in 4 cases, vesical calculi in 7 cases, and urethral calculi in 1 case. Although stricture of the urethra follow-

<sup>58</sup> Stevens, W. E. Diseases of the Urinary Tract During Infancy and Childhood, *J. Urol.* **23**: 61 (Jan.) 1930.

ing gonorrhea is rare in children, congenital strictures or stenoses in both sexes are not uncommon. They occur usually at the external meatus.

The same urologic procedures that are used in adults are indicated for the diagnosis and treatment of diseases of the urinary tract in infants and children. Postponement of treatment often results in permanent injury to the kidneys or other urinary organs. The general practitioner, pediatrician and urologist should cooperate to the utmost in the investigation and treatment of pathologic conditions of the urinary tract during infancy and childhood.

#### ENURESIS

Horton<sup>59</sup> reviewed the subject of enuresis and its treatment, particularly with reference to cases occurring in families compelled by economic circumstances to live in small crowded homes, where the problem presents, in addition to clinical aspects, a sociologic side. Five per cent of the total number of children attending the Children's Out-Patient Section of the London Hospital in one year suffered from enuresis.

In a study of 60 cases an endeavor was made to discover any common factor in its incidence and to attempt to obtain a quicker response to treatment by simple psychologic methods in conjunction with the use of belladonna. There were 23 boys and 37 girls in the series, 56 per cent of these were aged between 5 and 8 years on their first examination. Fifteen per cent of the children were aged more than 9 years, and 28.4 per cent were between 3 and 5 years. In 41.6 per cent of the cases enuresis dated from infancy and in 57.4 per cent the onset occurred after control of urination had been established over varying periods, from one month to seven years. A family history of enuresis was given in 56.6 per cent of the cases, in two cases enuresis had been present in the grandparents.

Various diseases occurred directly antecedent to the onset of the trouble. A rheumatic history was given in 13 per cent of the cases. Six cases dated from an attack of measles and 4 originated in severe frights. The symptoms were anorexia, restless sleep, insomnia, night terrors, constipation and headache. A complete general examination did not reveal abnormality in 48.3 per cent of the cases, there were varying degrees of general debility in the majority of these. Enlarged tonsils were found in 23.3 per cent and thread worm in 8.3 per cent, cervical adenitis occurred in a smaller proportion. Phimosi was present in only 1 case. Urinalysis was negative in the majority of cases.

<sup>59</sup> Horton, Kathleen M. Enuresis in Hospital Practice. *Arch. Dis. Child.* 1929; 4: 105 (April).



Patients with incontinence by day constituted only 5 per cent of the total group. Thirty per cent of the patients had enuresis only at night. It was about equally distributed between boys and girls. Enuresis was present both day and night in 55 per cent of the series. In 10 per cent of the cases incontinence of feces was associated with enuresis.

The following plan of treatment was carried out: regular weekly attendance for a considerable time and regular administration of the medicine. The child is not to be worried, scolded or punished. Tea, coffee, cocoa, soups, broths and meat extracts are not given. No more than four small cups of milk, milk and water or water alone are to be taken in the twenty-four hours. No drink is taken after 5 o'clock in the evening, slices of lemon or orange may be sucked for thirst. Salt fish or highly seasoned food are avoided, as well as heavy puddings and much potato. The child is put to bed early, on his side, and tight bed-clothes and a hard mattress are used. Urination should be at regular intervals and at the same time each day. The physician's share in the treatment consists in the correction of any local irritation, for example that due to urine, constipation, thread worms and drugs. The number of dry days and nights for each week are recorded, and unlimited opportunity for voluntary micturition during school hours is offered. Intake of fluid is increased gradually after complete freedom from enuresis, has been obtained for a month. Tincture of belladonna is given, beginning with 5 minims (0.3 cc) three times a day and increasing by weekly increments of 5 minims up to 30 or 35 minims (1.9 or 2.2 cc), with ammonium bromide 5 grains (0.32 Gm) three times a day, increasing by 1 or 2 grains (0.065 or 0.13 Gm) each week up to 12 grains (0.78 Gm). Tincture of nux vomica in doses of 2 or 3 minims (0.12 or 0.18 cc) is sometimes added to the mixture. The dose of the belladonna and bromide mixture necessary to help the child to secure seven dry days and seven dry nights is maintained for a fortnight and then reduced by the same amounts as it had been increased.

The results obtained by this treatment were very satisfactory. Sixty-five per cent of the patients were cured, whereas the remaining 35 per cent all showed improvement. The diurnal trouble cleared up six weeks from beginning of treatment. The nocturnal trouble cleared up in the same length of time in half of the cases, the remaining half was composed of cases in which attendance was not satisfactory. Complete recovery from both day and night enuresis was sometimes delayed as long as the eighteenth week.

## ADENOID CYSTIC CARCINOMA

GENERALIZED METASTASES IN THREE CASES OF BASAL CELL TYPE\*

J W SPIES, M D

NEW HAVEN, CONN

Some question has existed as to whether the tumors occasionally designated as adenoid cystic basal cell carcinoma are entitled to a special category. For the most part, the confusion has arisen regarding the relationship of this type of neoplasm to the following cutaneous diseases: epithelioma adenoides cysticum of Brooke and Fordyce, cystic rodent ulcer and the typical basal cell carcinoma as described by Krompecher. One must also distinguish adenoid cystic carcinomas from adenocarcinomas.

Certain tumors from both *cutaneous* and *noncutaneous* sites, presumably arising from basal cells or their derivatives, possess unmistakable adenoid cystic features. Since such tumors may be classed as basal cell carcinomas, there is a general tendency to minimize their lethal qualities. The loss of life occasioned by their possible widespread dissemination, or by direct extension into internal parts, is a point that I wish to emphasize and which induces a review of the subject at this time.

For the sake of convenience and clarity, this paper has been divided into three sections: (1) a review of the pertinent literature, (2) the presentation of data gathered from cases at the Memorial Hospital of New York and (3) a description of instances in which widespread metastases arose, a result apparently not anticipated in this type of tumor.

### RESUME OF THE LITERATURE

Although Krompecher,<sup>1</sup> in 1900, described the adenoid carcinomas of the skin and mucous membranes, it was not until 1903<sup>2</sup> that his

Submitted for publication, Feb 15, 1930

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†A preliminary report was presented before the New York Pathological Society on Oct 11, 1928. In an abstract that appeared in the *Archives of Pathology* (7:191 [Jan] 1929) the term roentgen therapy was erroneously substituted for irradiation therapy. The latter is a more general term and includes radium as well as roentgen therapy. The publication of the article has been withheld in order to make the follow-up more complete on case 3 (see detailed case reports of generalized metastases).

1 Krompecher, E. Der drusenartige Oberflächenepithelkrebs, Beitr z path Anat u z allg Path 1:28 1900

2 Krompecher, E. Der Basalzellenkrebs, Jena: Gustav Fischer 1903

notable contributions concerning basal cell cancer were collected into a single monograph. In this work he took up the task of definitely establishing a place for this group of carcinomas. So far as the skin is concerned, his conclusions have stood the test of time and have been generally accepted. There still remain many dissenting opinions as to other sources (mucous membranes, mammary glands, prostate, renal pelvis and salivary glands).

Krompecher recognized types such as solid, adenoid, cystic and keratinizing and combinations of these. He believed that not only the tumor cells but also the stroma might undergo a hyaline or a mucoid degeneration. He went so far as to remark that some basal cell carcinomas might show a similarity to adenocarcinomas, and no doubt it is due to this resemblance that many of the adenoid cystic carcinomas arising from *noncutaneous* sources are labeled with the histologic diagnosis of adenocarcinoma.

In describing twenty-five cases, Krompecher noted that five contained some squamous features. Except in one patient, however, there were no metastases. Of the remaining twenty, adenoid arrangement was disclosed in six, and five were of the cystic type. The cysts seemed to be the result of horny degeneration, sebaceous gland dissolution, caseous softening of basal cell masses, disintegration of the connective tissue which had been enclosed by the epithelial cells or malformed blood vessels and hair follicles.

Of the case reports, there were three that were interesting. The first patient had a primary carcinoma of the buccal mucous membrane with distant metastases. But there was some horny material in the center of the cell nests, and so it may have been a very cellular, anaplastic, squamous carcinoma. The second patient had a primary carcinoma of the nasal mucous membrane. There were local recurrences after each of two operations, and the process then extended to the frontal and sphenoidal sinuses. Exophthalmos became marked, and death resulted from meningitis. Autopsy was not performed, but the lymph nodes were considered free. Sections of the primary tumor showed a carcinoma of the solid basal cell type. The third case was of interest in that it showed at least two primary tumors, one being above the right eye and the other in the middle of the forehead.

With Krompecher's work as a general basis, it is deemed advisable for the remainder of the résumé, and during the analysis of cases, to divide the material into a *cutaneous* and a *noncutaneous* group. It is well realized that a vast and complicated literature has arisen in connection with tumors arising in or near the skin, and all that can be hoped for in an article of this length is to sift out a few of the important points. Moreover, it is clearly understood that, although certain

characteristics may warrant it, such tumors arising from *noncutaneous* portions of the body are not uniformly accepted by many pathologists as basal cell carcinomas

#### CUTANEOUS GROUP

In 1885, Balzer and Ménétrier<sup>3</sup> reported a case which they thought was one of adenomas of the sebaceous glands, but which has since been generally accepted as coming within the category of adenoid cystic epithelioma. One year later, Balzer and Grandhomme<sup>4</sup> presented a somewhat similar case.

In 1887, Jacquet and Darier<sup>5</sup> recorded the case of a man, aged 26, whose chest and arms were the seats of tumors varying in size from the "head of a pin to a pea." The tumors had been present for eighteen years. Darier thought that they were adenomas derived from sweat glands and that the material within the cysts was of a colloid nature. Accordingly, the term *hydradénomes éruptifs* was employed. Subsequently, at the International Congress of Dermatology and Syphilology in 1889, Quinquad<sup>6</sup> presented a case of the same general type. He sought a new terminology and arrived at that of *cellulome épithélial éruptif*. At the same meeting, Jacquet<sup>7</sup> discussed Quinquad's case and also mentioned Besnier and Unna as each having reported one case. Jacquet advanced the opinion that the lesions developed from embryonic epithelium of an indifferent nature, which had been misplaced during fetal life and was later excited into active proliferation. To the disease he gave the name *épithéliome kystique bénin de la peau*.

In addition to those mentioned a few other case reports were published, so that by 1892 the stage was well set for the excellent articles of Brooke and Fordyce, each of whom worked and wrote independently. Brooke<sup>8</sup> selected the term *epithelioma adenoides cysticum* and reported his observations on four cases, in two of which microscopic sections were made. Three of the cases occurred in a mother and her two daughters, aged 50, 18 and 14 years.

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3 Balzer, F., and Menétrier, P. *Etude sur un cas d'adenomes sebaces de la face et du cuir chevelu*, Arch de physiol norm et path 6 565, 1885

4 Balzer, F., and Grandhomme. *Nouveau cas d'adenomes sebaces de la face*, Arch de physiol norm et path 8 93, 1886

5 Jacquet, L., and Darier. *Hydradenomes éruptifs*, Ann de dermat et syph 8 317, 1887

6 Quinquad. *Cellulome épithélial éruptif*, Ann de dermat et syph 8 412, 1887

7 Jacquet, L. *Epithéliome kystique bénin de la peau* Compt rend Cong internat de dermat et syph 1889, p 416

8 Brooke, H. G. *Epithelioma Adenoides Cysticum*, Brit J Dermat 4 269, 1892

The lesions had appeared between the ages of 10 and 14 years and consisted of tumors projecting slightly above the surrounding skin and ranging in size from 1 mm to one-half of a small pea. They had soon grown dark and exhibited a shiny, translucent covering of skin. Nearly all contained one or more milia which were plainly visible to the unaided eye. The size of the milium bore no relation to the size of the tumor. The papules seemed to be intradermal and felt firm but not hard. The lesions were scattered thickly about the nose and eyebrows, thinly on other places and none was seen on the lower limbs. Brooke stated that their course was always slow, but that they might take on a sudden acceleration after many years. According to his cases and those of other workers, neither spontaneous involution nor ulceration had ever been observed. The symptoms, if any, were those of a slight pruritus.

Brooke's microscopic observations are worth repeating. The cysts, which were circular or oval, were filled with a colloid material or with concentric layers of horny epithelium. Their size varied so that some could be detected only with the high power of the microscope, while others were prominent with the low magnification. The cysts were formed from degenerating foci of tumor cells. As this process continued, the cells on the periphery grew more and more flattened. In many places there was thus formed a distinct membrana limitans. Some of the cell masses were separated from the connective tissue by a layer of palisade-like cells which stained more darkly than the rest of the growth. Brooke thought that limitation in the growth of the tumor nodule might be due to a peculiar capsule-like structure formed by the connective tissue.

Fordyce's contribution<sup>9</sup> was equally important. He presented two cases, in a mother and her daughter. In addition to the observations which Brooke had made, Fordyce noted a central depression in a few of the growths. Pigment spots and telangiectases were also seen.

In his histologic description, Fordyce mentioned the strong resemblance of the cell masses to adenomas. The individual cells were similar to those seen in the lower layers of normal epidermis. Linear tracts (formed by two or more cells in width) coursed through the derma, intermingled in a most complicated way and connected the large cell masses with one another. Some of these strands resembled coil gland ducts, but no lumen could be made out. The cysts were either empty or else contained keratohyaline material, deeply pigmented detritus or loose degenerating cells. Some cysts were difficult to distinguish from glands, but they lacked the external limiting membrane. Cysts could be found in the connective tissue without apparent con-

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<sup>9</sup> Fordyce, J. A. Multiple Benign Cystic Epithelioma of Skin, *J. Cutan & Genito-Urin Dis.* **10** 459, 1892.

nection with any other structures. The beginning of cystic formation was evident in the central portion of some of the tumor masses. There the cells were extremely pale, often imperfectly stained, and at times only the rim of the nucleus could be seen.

In those tumors which had a central depression, Fordyce could trace a direct connection with the lower layers of the epidermis, and the outer cells of the hair follicles were proliferating. The sebaceous glands seemed independent of the process.

One case of lupus erythematosus and another of rodent ulcer were shown in order to emphasize the close histologic picture between these and multiple benign cystic epithelioma, which was Fordyce's appellation for the disease. He concluded that a distinction can properly be made only from the clinical observations together with the natural history of the disease.

From this point many observers were stimulated into reporting cases, and consequently there developed an extensive literature. I think, however, that with the exception of Savatard's article in 1922, the abstracting of such would be superfluous. I therefore refer the reader to the articles themselves. Henceforth, as a rule, only new or important supporting observations will be given.

Heidingsfeld,<sup>10</sup> in a study devoted to the transitional morphology of benign epitheliomas, expressed the belief that the cysts were formed as a result of colloid degeneration of the tumor cells. Sutton<sup>11</sup> wrote that there were two kinds of cysts in multiple basocellular carcinoma. The primary type was due to degeneration of the epithelial cells and the secondary type was derived from the degeneration of connective tissue which had been enclosed by the epithelial tumor cells. Furthermore, he found colloid degeneration of connective tissue outside of such areas. At a later date, Hazen<sup>12</sup> confirmed the finding of a colloid-like material in the majority of the cysts.

Savatard<sup>13</sup> reported fourteen new cases. One patient of great interest was the elder daughter described by Brooke thirty years before. The disease had steadily progressed. By this time there were large lumpy patches, and some of the single lesions were "as large as a cherry." There was a distinct tumor nodule on the calf of the left leg. It will be recalled that Brooke had emphasized the small size of the lesions.

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10 Heidingsfeld, M. L. Benign Epithelioma. A Study of Transitional Morphology, *J. A. M. A.* **59** 256 (July 27) 1912.

11 Sutton, R. L. The Histogenesis of Multiple Basocellular Carcinoma. *J. A. M. A.* **62** 977 (March 28) 1914.

12 Hazen, H. H. Skin Cancer, St. Louis: C. V. Mosby Company, 1916, pp. 61, 102 and 103.

13 Savatard, Louis. Epithelioma Adenoides Cysticum. *Brit. J. Dermat.* **34** 381 1922.

and their absence from the lower limbs. None of the growths had ulcerated or involuted.

The existence of adenoid cystic epithelioma in the negro race was reported by Sutton<sup>14</sup>. His patient had a remarkable family history. The hereditary nature of the disease has been unmistakable in some well authenticated cases, and in others it has been definitely absent. One can find numerous instances supporting either side of this question.

Ulceration of the supposed benign lesions was early observed by Jarisch<sup>15</sup> and confirmed by Little,<sup>16</sup> Savatard,<sup>13</sup> Dore<sup>17</sup> and others. In Dore's case the lesion may have been malignant.

It is probably true that some of the benign tumors had broken down without showing unrestrained growth, yet on the other hand, practically all of the malignant lesions had an associated or a preceding ulceration. As early as 1890, Hallopeau,<sup>18</sup> reporting what he believed was a case of tumors of sweat gland origin, but which later authors have thought was adenoid cystic epithelioma, mentioned that among the innocent lesions was one that appeared malignant. A section was taken and it was examined by Darier, who pronounced it to be a malignant epithelioma. Four years later a similar observation was made by J. C. White,<sup>19</sup> who noted that coexisting with the benign forms were several broken down skin cancers. Some of these appeared to resemble Hutchinson's crateriform epithelioma, while others seemed to be rodent ulcers. White thought that they had probably originated in the benign lesions, and he ventured to predict that many would undergo such changes if a sufficient period of time was allowed to elapse. These observations were later given adequate support by Hazen,<sup>12</sup> Stelwagon<sup>20</sup> and others. Savatard<sup>13</sup> apparently had such a case which recurred after operation, and he quoted Cranston-Low as citing the case of a patient whose lesions had undergone malignant transformation.

Why innocent tumors should change their character and begin an invasion which threatens the patient's life is an unsolved problem.

14 Sutton, R. L. A Differential Study of Multiple Benign Cystic Epithelioma and Adenoma Sebaceum in the Negro, *J. Cutan. Dis.* **29** 480, 1911.

15 Jarisch. Zur Lehre von den Hautgeschwulsten, *Arch. f. Dermat. u. Syph.* **28** 163, 1894.

16 Little, E. C. G. A Note on Two Cases of Epithelioma Adenoides Cysticum (Brooke) Tricho-Epithelioma, *Brit. J. Dermat.* **26** 173, 1914.

17 Dore. Multiple Benign Cystic Epithelioma (One Case), *Brit. J. Dermat.* **24** 190, 1912.

18 Hallopeau, M. Hydradenoma complique d'epithelioma vulgaire, *Ann. de dermat. et syph.* **1** 872, 1890.

19 White, J. C. Multiple Benign Cystic Epithelioma (One Case), *J. Cutan. & Genito-Urin. Dis.* **12** 477, 1894.

20 Stelwagon, H. W. Treatise on Diseases of the Skin, ed 9, Philadelphia, W. B. Saunders Company, 1921, pp 680 and 908.

White<sup>19</sup> thought that it might be accounted for by changes associated with the age of the patient, or that it might be due to the invasion of normal cutaneous epithelium which reacted against the tumor in an abnormal way. The line between benignancy and malignancy is often very narrow as was recognized by Sutton,<sup>21</sup> who reported cases in a mother and daughter. Each had many lesions representative of benign cystic epithelioma. In addition, the mother had a rodent ulcer near the eye where there had been no preexisting lesion, in the daughter, one had developed in a benign lesion on her neck. Sections from the rodent ulcer and from three of the benign lesions had the same histologic picture and would ordinarily have been diagnosed as rodent ulcer.

The origin of tumors belonging to the "adenoid cystic group" will be treated briefly. Most authors have agreed that in all probability they arise from the basal cell layer of the rete pegs or from the sheath of a hair follicle (Wolters,<sup>22</sup> Hartzell,<sup>23</sup> Hazen<sup>12</sup> and others). Heidingsfeld<sup>10</sup> believed that the tumor cells were of a distinct basal cell character, but that any macroscopic lesion had proceeded too far for its genesis to be traced by a microscopic study. He found that structures in the immediate neighborhood of the tumor were undergoing proliferation and that he attributed to a "stimulus beyond the recognizable sphere of morphologic change."

That the skin tumors known as adenoid cystic epitheliomas might often be confused or associated with other lesions was supported by Pick<sup>24</sup> (acne rosacea with adenoma sebaceum), Sequera<sup>25</sup> (lupus erythematosus) and Savatard<sup>13</sup> (moles). Although the characteristics of this malady have become more clearly defined, there still exists an uncertainty in the minds of some observers. Adenoma sebaceum has been definitely separated, leaving rodent ulcer and syringocystadenomas (the latter to a lesser degree) as the principal diseases to consider in the differential diagnosis.

In this connection it is well to recall that Hallopeau<sup>18</sup> reported his case as hydiadenomas (syringocystadenomas). In a differential study

21 Sutton R. L. Occurrence of Cancerous Changes in Benign New Growths of the Skin, *Am J M Sc* **145** 819, 1913

22 Wolters Epithelioma Adenoid Cysticum, *Arch f Dermat u Syph* **56** 89, 1901

23 Hartzell, M. B. Benign Cystic Epithelioma and Its Relationship to So-Called Syngo-Cystadenoma, Syngocystoma, and Haemangio-Endothelioma, *Brit M J* **11** 991, 1904

24 Pick Ueber das Epithelioma adenoides cysticum (Brook) und seine Beziehung zum Adenom der Talgdrusen (Adenoepitheliom), *Arch f Dermat u Syph* **58** 201, 1901

25 Sequera Epithelioma Adenoides Cysticum (Report of 4 Cases), *Brit J Dermat* **26** 89 1914



between this disorder and adenoid cystic epithelioma, J C White<sup>26</sup> observed that tumors of sweat gland origin were smaller at high altitudes than at sea level, and that at any given height the sweat secretion was less in the tumor area than in the normal adjacent skin. Histologically, the process appeared to be due to the growth and cystic dilatation of the ducts rather than of the sweat glands proper. In a study of similar purpose, Sutton and Dennie<sup>27</sup> found that the administration of pilocarpine would increase the size of the true syringocystadenomas. Schidach<sup>28</sup> was able to mimic the tumor process of sweat glands by experimentally occluding the ducts. In the proliferation of the cells thus stimulated, he discovered budding processes and distinct cysts. Therefore, it would appear from these and other studies that tumors of sweat gland origin are probably distinct from "adenoid cystic epitheliomas" found arising from the sheath of hair follicles and the lower basal layer of covering epithelium.

TABLE 1—*Points of Difference as Listed by Adamson*

<i>Rodent Ulcer</i>	<i>Adenoid Cystic Epithelioma</i>
Usually in males	Usually in females
Occurs in later life	Appears in childhood
Not hereditary	Distinct familial tendency
Irregular distribution	Symmetrical distribution
Varying size, no limit	Uniform size, limited
Locally malignant	Not locally malignant

Many interesting discussions have taken place concerning the relationship between rodent ulcer and adenoid cystic epithelioma. There are still some authors who class the two together.

In a differential study directed toward the separation of these two diseases, Adamson,<sup>29</sup> as early as 1908, concluded that the cases reported as adenoid cystic epithelioma by Stelwagon and Jarrisch were really rodent ulcers. He believed that the one recorded by White was either a true rodent ulcer or a connecting link between the two disorders. Table 1 lists the chief points of difference as given by Adamson.

Six years later, Adamson<sup>30</sup> reemphasized that rodent ulcers, beside their tendency to ulcerate, usually appeared late in life. In a second

26 White, J C. Syringocystoma, *J Cutan Dis* **49** 49, 1907.

27 Sutton, R L, and Dennie, C C. Possible Interrelationship of Acanthoma Adenoides Cysticum (Multiple Benign Cystic Epithelioma) and Syringocystadenoma (Lymphangioma Tuberosum Multiplex), *J A M A* **58** 333 (Feb 3) 1912.

28 Schidach, Tominatsu. Experimentelle Erzeugung von Hidrocystomen, *Arch f Dermat u Syph* **83** 3, 1907.

29 Adamson, H G. Two Cases of Multiple Rodent Ulcer, *Lancet* **2** 1133, 1908.

30 Adamson, H G. On the Nature of Rodent Ulcer, *Lancet* **21** 810, 1914.

paper written the same year,<sup>31</sup> he mentioned the similarity between multiple rodent ulcer and adenoid cystic epithelioma

The points of difference listed by Adamson warrant discussion

Whether the patient is a male or a female has not been found of sufficient importance to stress

Sequera<sup>25</sup> stated that the age distinction was not reliable, for rodent ulcers could start early in life (he reported one case in which the age was 11 years) and were usually confused with lupus vulgaris. Likewise, the appearance of adenoid cystic epithelioma at a later age than commonly thought was supported by Dyer<sup>32</sup> and Hartzell.<sup>33</sup> Ormsby,<sup>34</sup> however, wrote that the occurrence of rodent ulcer at a usually later age was of distinct value in the diagnosis.

The familial tendency of adenoid cystic epithelioma is of some importance and has already been mentioned.

Cases of patients with single lesions of the benign disease have been reported by several investigators. Wolter's case<sup>22</sup> was apparently the first recorded. Savatard<sup>13</sup> concluded that the solitary form of the disorder was more frequent than the multiple variety, but that it was usually overlooked. He quoted Cranston-Low's somewhat analogous observations. Various authors have noted multiple forms of rodent ulcer. However, despite the fact that single and multiple lesions occur in either disease, it is probable that symmetry of distribution in the multiple form points toward adenoid cystic epithelioma.

It has been generally conceded that the benign disease has a greater tendency to uniformity in size and to limitation in growth, but even here exceptions have been reported.

The presence of malignant changes and of ulceration in adenoid cystic epithelioma has already been touched on. Sutton<sup>21</sup> believed that one could depend neither on the ulceration of a lesion nor on the histologic picture to separate one type of neoplasm from the other. Little<sup>16</sup> added to the complexities of the subject by reporting two cases of what he believed to be adenoid cystic epithelioma with ulceration of some of the lesions. In a later article,<sup>35</sup> he mentioned Bland-Sutton as having diagnosed the two conditions in mother and daughter when Little thought that despite the ulcerations both had the benign and not the malignant disease. In contrast to Little's belief, Johnston and

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31 Adamson, H. G. Epithelioma Adenoides Cysticum or Brodie, *Brit. J. Dermat.* **26** 88, 1914.

32 Dyer, I. Multiple Benign Cystic Epithelioma. *Am. J. Dermat. & Gcnito-Urin. Dis.* **1-2** 52, 1897-1898.

33 Hartzell, M. B. Benign Cystic Epithelioma. Report of Two Cases Presenting Unusual Features, *Am. J. M. Sc.* **124** 441, 1902.

34 Ormsby, O. S. Diseases of the Skin, ed. 3 Philadelphia, Lea & Febiger 1927, p. 666.

35 Little, E. G. C. Rodent Ulcer, *Brit. J. Dermat.* **27** 145 1915.

Paul <sup>36</sup> in the same year reported a case in which on account of the ulcerations the diagnosis of multiple rodent ulcer was made. They were willing to concede, however, that their case might be one of the so-called connecting link types. Miller <sup>37</sup> reported four cases under the title of benign cystic epithelioma, one of which presented ulcerations. This patient died one year later with bronchopneumonia. It is unfortunate that no autopsy was performed.

Little <sup>35</sup> maintained that the chief distinction between rodent ulcer and adenoid cystic epithelioma was that the former was rare except on the face, but he admitted that extrafacial cases of rodent ulcer had been reported.

Stelwagon <sup>20</sup> listed twelve synonyms for benign cystic epithelioma, these being given in French, German and English. He noted its close relationship in structure to rodent ulcer and reiterated the fact that malignant changes might be superimposed. Therefore, he thought that the prognosis was not always certain.

In contrast with the foregoing authors, others have thought it not uncommon for rodent ulcers to undergo cystic degeneration and thus to present a distinct type. In 1901, Dubreuilh and Auché <sup>38</sup> described such a process. They, together with Hazen,<sup>12</sup> believed that the cysts might be formed from the degeneration of the tumor cells resulting in keratohyaline changes. They observed that sometimes the cavities were very large and numerous. Cystic rodent ulcers have been described by other authors. As late as 1927 Ormsby <sup>34</sup> stated that cystic degeneration of basal cell carcinoma might occur.

It can readily be seen that confusion still exists, and that the separation of adenoid cystic epithelioma and cystic rodent ulcer is sometimes a matter of personal opinion. In two papers <sup>39</sup> Hartzell proposed that the various skin tumors which possessed similar histology should be placed in one group until more accurate studies could be made.

*Do Basal Cell Carcinomas Metastasize?*—Another question of absorbing interest has been whether a true basal cell carcinoma had the power to metastasize. It has generally been thought that they do not. There are some well authenticated cases, however, which lead one to believe that there are possible exceptions to the rule, yet it is reasonable to suppose that some of these may be accounted for by the fact that some predominantly basal cell carcinomas may contain a few squamous

<sup>36</sup> Johnston and Paul. Multiple Rodent Ulcer, *M. J. Australia* **2** 139, 1915.

<sup>37</sup> Miller, J. W. Multiple Benign Cystic Epithelioma, *J. Cutan. Dis.* **33** 462, 1915.

<sup>38</sup> Dubreuilh, W. and Auché, B. De l'ulcus rodens, *Ann. de dermat. et syph.* **2** 705, 1901.

<sup>39</sup> Hartzell, M. B. Benign Cystic Epithelioma and Its Relationship to So-Called Syringo-Cystadenoma, Syringocystoma, and Haemangio-Endothelioma, *Brit. J. Dermat.* **16** 361, 1904, footnote 23.

elements, as Broders and MacCarty<sup>40</sup> have pointed out. They wrote that basal cell carcinomas could be found on any surface of the body covered by protective epithelium, and that the lesions presented great variations in cell morphology and arrangement. They were either alveolar, glandlike (even resembling thyroid tissue) or in solid masses, and some might also present combinations of these forms. Prickle cells could be rarely but positively demonstrated. A certain number of basal cells could always be demonstrated in squamous cell carcinoma. As a matter of fact, Broders and MacCarty seemed to think that all tumors arising in protective epithelium came from the basal cell layer and the only feature that distinguished them was their cellular differentiation. Stelwagon<sup>20</sup> made notation to the effect that there was a rare possibility of rodent ulcer involving lymph glands, and that its type might be changed into a deep-seated or papillary form of the disease. In an excellent article on cancer of the skin, Morton<sup>41</sup> pointed out that basal cell carcinoma might conceivably give rise to regional metastases.

Beadles<sup>42</sup> reported a case which presented an extensive rodent ulcer of fifteen years' duration, situated on the upper part of the face, and in which there was definite extension to the lymph nodes beneath the lower jaw. The histology was described as being glandular. There were no solid masses or keratinoid areas. Two years before a similarly involved node had been removed from the neck. There was no invasion of the capsule. Death resulted from septic pneumonia. Dubreuilh and Auché<sup>38</sup> observed a patient who had a rodent ulcer situated on the brow, nose and eyelid, which apparently involved the regional lymph glands. Fordyce<sup>43</sup> recorded the case of a man, aged 60, who had a typical rodent ulcer of ten years' standing. It extended from the side of the nose to the inner canthus of the eye. Coincident with this there was a somewhat similar condition behind the ear. The latter lesion was operated on, and there was a recurrence in the scar. Following this, a lymph node in the region of the mastoid process became enlarged and the microscopic appearance was identical with that of the primary tumor. Fordyce sought to explain this unusual extension of the disease by the fact that the tumor, situated between bone and dense fibrous tissue, had considerable pressure exerted on it which may have forced some of the cells into the lymphatics. Korb<sup>44</sup> reported two

40 Broders, A. C., and MacCarty, W. C. Epithelioma, *Surg. Gynec. Obst.* **27** 141, 1918.

41 Morton, John T. Cancer of the Skin, *Arch. Surg.* **12** 655 (March) 1921.

42 Beadles, C. F. Rodent Ulcer, *Tr. Path. Soc. London* **45** 176 1894.

43 Fordyce, J. A. Cancer of the Skin. I. Cutan. & Genito-Urin. Dis. **20** 147, 1902.

44 Korb, H. Die Röntgenbehandlung der Haut Carcinome speciell des Basalzellenkrebs, sein histologisches Verhalten vor und nach der Bestrahlung. *Arch. klin. Chir.* **97** 752 1912.

cases of rodent ulcer which apparently metastasized to adjacent lymph glands. One underwent squamous metaplasia in the lymph node, but the other case retained its pure basal cell character.

It is a singular fact that Hazen<sup>45</sup> should report four cases within one year after he had stated in his textbook that basal cell carcinoma never metastasized and that when glands were reported as involved, there had probably been an error in the diagnosis.<sup>12</sup> In view of the data given, however, only one of Hazen's cases can be fully accepted. In this patient there had been a history of seven years' previous treatment which had resulted in successive healings and subsequent recurrences. No changes in histology were noted, however, and the metastatic tumor was an unmixcd basal cell carcinoma. Finnerud<sup>46</sup> had two patients who suffered from basal cell carcinoma of long standing. The lesions had been treated with satisfactory primary results but had repeatedly recurred. Finally, both metastasized to the submaxillary space. Each presented the microscopic picture of basal cell carcinoma in the primary and secondary growths. In the tissue from one of the patients there were distinctly cystic areas.

From the foregoing, it would seem that basal cell carcinoma may rarely extend to the regional lymph nodes. It is hard to ascertain whether any of the reported cases were of the adenoid cystic type, but it would appear that at least two (Finnerud's and Beadle's) may have belonged to that group.

After a careful search through the literature, I have been unable to find any case in which definite, unmixcd, basal cell carcinomas arising from the skin gave rise to widespread or distant metastases.

#### NONCUTANEOUS GROUP

Since a mass of conflicting literature has collected on the subject, and in consideration of certain cases analyzed and reported herein, I wish to emphasize the fact that some eminent pathologists believe that basal cell carcinomas (some of which are of the adenoid cystic type) may arise in places other than the skin.

No attempt will be made to cover fully the literature. The third edition of Ewing's "Neoplastic Diseases"<sup>47</sup> will be the chief source for reference.

45 Hazen, H. H. Basal Celled Cancers of the Skin, South M. J. **10** 241, 1917.

46 Finnerud, C. W. Metastatic Basal Cell Carcinoma from the Skin, J. A. M. A. **82** 775 (March 8) 1924.

47 Ewing, James. Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928.

The maxillary sinus and the nasal mucosa may give rise to carcinoma of the basal cell type. The structure may simulate that of the thyroid gland, or a more compact arrangement may resemble that of adenoid cystic carcinoma. As a rule, the growth is slow, recurrence is persistent after incomplete excision and there may be extension to lymph nodes or bone.

Some of the malignant tumors of the salivary glands are of the basal cell type. It is true as Krompecher<sup>2</sup> stated that some neoplasms of the mucous membrane and other structures as well belong within this group, and some of these in turn may be placed into the adenoid cystic subdivision. The structure and clinical course may follow that of tumors of similar appearance but which arise from the skin. Misplaced bits of epithelium may serve as the source for such growths. These may lie in the orbit, lacrimal duct, buccal mucosa and elsewhere. At times they are confused with endothelioma or adenocarcinoma.

In 1901, Buxton<sup>48</sup> reported a case from the Memorial Hospital in which the tumor had originated at the orifice of Steno's duct. After running a slow course for twenty years, it metastasized to the regional lymph nodes. The histology of the primary and secondary growths was that of adenoid cystic basal cell carcinoma.

In 1916, New<sup>49</sup> called attention to what may have been a similar case. He did not express such an opinion, however, and made no mention of metastasis. In 1918, Broders and MacCarty<sup>40</sup> wrote that some tumors of the palate are composed of cysts, glands and squamous epithelium in varying amounts. In 1919, Broders<sup>50</sup> stated that some tumors arising in the nose, pharynx, antrum, parotid gland, mouth and similar places looked like basal cell carcinoma, but that the trained eye will detect a difference. Just what this difference was, he did not clearly state. He also referred to the fact that the lesions would metastasize, but, again, this was a general notation without being supported by definite personal cases or by reference to other authors. He placed stress on the variations in the histologic structure and expressed the belief that basal cells might take on squamous features.

In 1922, Johnson,<sup>51</sup> from the Memorial Hospital, New York, described seven cases of what he termed aberrant adenoid cystic epi-

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48 Buxton, B. H. *Benign Epithelial Tumors of the Skin*, Pub. Cornell Univ. M. Coll. Stud. Dept. Path., 1901-1902, vols. 1-2, sect. 5.

49 New, G. B. *Adenoma of the Palate*, *Ann. Otol. Rhin. & Laryng.* **25**: 687, 1916.

50 Broders, A. C. *Basal-Cell Epithelioma*, *J. A. M. A.* **72**: 856 (March 22) 1919.

51 Johnson, F. M. *Aberrant Adenoid Cystic Epithelioma of the Salivary Gland Type*, *Ann. Surg.* **75**: 331, 1922.

thelioma of the salivary gland type. Five were from the palate, one arose from the skin of the upper lip and the other originated from the epidermis of the forehead. Their tendency was neither to ulcerate nor to involve lymph nodes. He thought that they were very amenable to irradiation therapy.

#### SUMMARY

A rather extensive review of the literature has been made. As a general basis for discussion, Krompecher's classic work on basal cell carcinoma is utilized. Following this, a distinction is made between the tumors of *cutaneous* and *noncutaneous* origin. In the former, an attempt is made to develop the idea that the first reports generally tended to deal with a benign process which occurred in the young, and often exhibited a familial tendency. The factor of ulceration is brought in and naturally leads into a discussion of rodent ulcer. Histogenesis and histology have both brought into the review a limited amount of space devoted to tumors arising from sweat glands or from sebaceous structures. The report of malignant changes reported by some authors has been considered and also the question of metastatic basal cell carcinoma has been dealt with. In the noncutaneous group the lack of uniformity of opinion has been stressed, and certain cases have been given space.

In no case in the literature has there been found a true instance of widespread dissemination of an unquestioned basal cell carcinoma.

#### ANALYSIS OF CASES

The fifty-eight cases used in this study were selected from a group comprising 185 basal cell carcinomas. These were from cutaneous sites, buccal mucosa, tonsil, nose and antium. Neoplasms resembling basal cell tumors histologically, but derived from such organs as the cervix or the esophagus, were not studied. Since these are highly malignant and are prone to metastasize readily, from a clinical standpoint they do not fit into the ordinary basal cell type. Furthermore, adenoid cystic forms of these tumors seem rare.

In order to follow the general tendency in past studies and on account of the marked difference in mortality, the adenoid cystic basal cell carcinomas were divided in two groups, *cutaneous* and *noncutaneous*.

#### CUTANEOUS GROUP

Thirty-seven cases occurred in this group. Seven of these had some squamous features, and they will be analyzed separately.

The age at which the lesion first appeared is given in table 2 in decades. This datum was obtainable in twenty-six cases.

The youngest age at which the lesion appeared was 26, and the oldest, 72 years. The average age throughout the series was 48 years. It will be seen that the ages follow closely those in which basal cell carcinomas of the rodent ulcer type are found.

Sixteen of the thirty cases were in females, and fourteen in males. Thus sex played no important rôle. Furthermore, nationality did not seem to have any bearing. In the twenty-six cases in which nativity could be determined it seemed to be evenly distributed among the types of people who patronized the hospital. Likewise, occupation assumed a negligible part. People engaged in outdoor pursuits were not as numerous as those who worked where their skin would be less exposed to the elements. This was further supported by the fact that women who naturally live indoors more than men, slightly outnumbered the men.

Only ten cases could be found in which there was even the slightest suggestion as to etiology. The apparent etiologic factors will be listed,

TABLE 2—*Age Incidence in Twenty-Six Cases of Cutaneous Group*

<i>Decade</i>	<i>Number of Patients</i>
3rd	2
4th	3
5th	12
6th	5
7th	3
8th	1

but no conclusions will be drawn. (1) eczematoid lesions treated twenty-two years before with arsenic, (2) a toofer developed a lesion in the postanal skin, (3) pince nez glasses caused irritation of the nose followed by formation of wartlike lesions which broke down, (4) a barber accidentally clipped off the top of an apparently benign wart which finally healed, but five years later a lesion appeared in about the same place, (5) a tumor developed in or near a scar which had resulted from a wound caused by a wooden splinter, (6) a burn in which incomplete epithelization took place, (7) a burn from a spark of fire which healed but in the scar of which a pimple formed, (8) pressure of eye glass frame on a benign mole of long standing, (9) a "pimple" which was squeezed, (10) a mole which was irritated by scratching. The foregoing factors are merely suggestive, and nothing definite can be deduced from them.

In adenoid cystic epithelioma of the skin competent observers have noted the familial nature of some of the cases, the general tendency of the lesions to remain stationary after slowly reaching 0.5 cm. or less in size and the usual lack of ulceration. The cases in the Memorial



Hospital exhibit no hereditary qualities, and the lesions have progressively spread unless controlled by treatment. In the group of thirty cases, ulceration was absent in five, not mentioned in five and present in twenty. In these twenty it was definitely spontaneous in thirteen, questionably so in four and caused by external agents in three. Therefore, one may assume that spontaneous ulceration in our cases was fairly characteristic of the disease.

Pain was present in only four cases, and then it was very mild. It was definitely absent in eighteen. In seven patients there was no reference to pain, and probably none existed. A slight itching sensation was noted in one case. Consequently, one is led to believe that pain is a negligible factor.

In general, the distribution of the lesions corresponded to that seen in the usual types of basal cell carcinoma. Most of them were located on or about the nose, there were many on or near the eyelids, and some were found on the forehead or adjoining temporal regions. Unusual sites were the forearm, back and neck (one case), buttock (one case), and neck, below and behind ear (one case).

When the disease progressed, it was by local extension. Eight of the thirty cases showed this to a rather marked degree. There was one case which invaded the skull, meninges and brain. Another case (not included in this study) has recently come to notice in which there is invasion of the mandible. Whether the neoplastic cells actively grow into living bone, or whether they merely replace devitalized osseous tissue which has been eroded and atrophied through pressure and infection is an unsettled point, it would appear, however, that the former process is the more probable.

The duration of the lesion before the patients came to the Memorial Hospital was ascertained in twenty-seven cases. The shortest interval was four months (one case), and the longest was thirty years (one case). The average was seven and one-half years. Because of failure to eradicate the lesions when they were small and amenable to treatment, large areas of tissue were destroyed with resulting mutilation, and the duration of the treatment was needlessly prolonged.

A follow-up study was made for at least three years in fifteen cases of unmixed adenoid cystic basal carcinoma, some cases were studied for a much longer period.

Previous treatment had been instituted in twelve of the fifteen cases and consisted in employing everything from salves to surgical intervention and irradiation. As nearly as can be judged, both surgical intervention and irradiation were exercised in a desultory manner. At least they proved effective in the Memorial Hospital under undoubtedly much worse conditions than when the patients first presented them-

selves elsewhere. It seems hardly possible to overemphasize the importance of adequate, early treatment.

In the therapeutic regimen at the Memorial Hospital, external irradiation (usually radium) was employed in every case. This was reinforced by interstitial applications in seven cases. In addition, surgical procedures, varying from the evacuation of the orbit to the excision of small areas of infected or tumor tissue, were employed in eleven cases. It is interesting to note that in all cases in which interstitial irradiation was used there was also surgical intervention. These cases were undoubtedly worse than those in which external irradiation alone sufficed. The number of treatments with irradiation varied from one to twelve, and in the series as a whole each patient had an average of four and one-half treatments. It is possible that the number of treatments could be reduced by employing the x-ray or large radium applicators (pack) instead of using radium in small applicators, for in that way it would be possible to treat a much greater area at one time. The underlying normal tissues, however, would receive more proportionate irradiation, and this would often be a contraindication (as in lesions near the eye or overlying bone). The number of surgical procedures varied from one to about three in each of the eleven patients submitted to them.

The duration of the treatment varied from the necessary requirement for application in two cases to five and one-half years in one case. The average duration for all of the cases taken collectively was two years and two months.

An analysis of the final results reveals that only one patient is known to have died. Her condition was obviously hopeless from the start. The lesion was of ten years' duration and had already destroyed a large part of the left parietal, temporal and frontal bones. She developed hernia cerebri, and this was followed by hemiplegia. Of the remaining fourteen patients, two were lost from observation after being free from apparent disease at the end of four months in one case and of nine years in the other. There were twelve patients alive. One had a definite recurrence after it seemed probable that the disease was controlled, this occurred five years after the first treatment. The subsequent lapse of time has been insufficient to estimate the permanent results of the final treatment. For the eleven patients alive and seemingly well, the period of observation at the Memorial Hospital has varied from three to eight and one-half years, and the average is more than five years.

When one considers the extent of the disease and its duration before treatment here, the results are satisfactory so far as the actual preservation of life goes. However, there were numerous recurrences, and in ten of the fifteen cases in which follow-up studies were made, there

were complications varying from loss of bits of tissue to that of an eye. Some of the patients had sequestrums. The complications could be avoided in only the early cases, and these unpleasant factors serve to strengthen the plea for earlier and more effective treatment.

*Mixed Squamous and Adenoid Cystic Basal Cell Carcinoma from Cutaneous Sites*—This group comprises seven cases. The squamous elements were marked in some and slight in others, but were definite in all cases. The adenoid cystic portion did not differ from that of the unmixed group analyzed. The occasional occurrence of two neoplastic elements in the same tumor is well known to pathologists, and therefore needs no elaboration.

There were five males and two females. Neither nationality nor occupation seemed to play any definite rôle. The age of the patient at the time the tumor appeared varied from 15 to 39 years. The duration of the lesion before the patient came to the Memorial Hospital varied from five to twenty years, with an average duration of nearly ten years.

For a possible bearing on etiology there might be mentioned one case in which there was irritation of a benign mole by scratching, in a second there was a form of benign lesion that had existed for years which was accidentally incised by a barber, and which on failure to heal was treated with hydrochloric acid, in a third case, the patient sustained a blow which resulted in a "scab" formation, being followed by a lesion that never healed. The remaining four cases had nothing in the least suggestive, and in these there was no preexisting lesion.

Ulceration was present in four cases and absent in three. In four cases that showed ulceration, the process was definitely spontaneous in one, questionably so in two and caused by external agents in the remaining one.

Pain was present in three of the seven cases, it seemed to be relieved by treatment.

In five of the patients the lesion was located on the nose, in one on the eyelid and in the other on the forehead. In five of the cases there was considerable local extension of the disease. In one case the temporal bone was destroyed and the meninges and brain were involved. In two of the cases the disease apparently extended little, if at all.

Only four of the cases have been followed-up for three years or more. Obviously, the number is too small to be of much value. Hence, only a few features will be mentioned.

All of the patients had had previous inadequate treatment with irradiation, and one had also been operated on. At the Memorial Hospital irradiation (external and interstitial) was employed in conjunction with surgical procedures. One patient died of extensive pulmonary tuberculosis (positive roentgenograms and sputum typical

clinical picture) and was apparently free from carcinoma. The patient with involvement of the meninges was lost from observation after being observed for one year and four months. His case was hopeless from the time of his first appearance at the Memorial Hospital, and he is doubtless dead. One patient is living and seems free from disease (observed for seven years and nine months). The fourth patient is living, but is in poor condition.

To justify the tremendous mortality, one must admit that when the patients arrived at the Memorial Hospital the disease was so extensive that the outlook was already hopeless.

#### NONCUTANEOUS GROUP

There are twenty-one cases in this group. Two of these have some squamous features and will be analyzed separately.

Table 3 gives in decades the ages at which the lesions were first noticed. Such data were obtainable in thirteen cases. The youngest patient was 35, the oldest, 76. The average age was 50 years.

TABLE 3—*Age Incidence in Thirteen Cases*

<i>Decade</i>	<i>Number of Patients</i>
4th	4
5th	2
6th	6
8th	1

Eleven of the patients were males, and eight were females. This slight preponderance of males may be explained by the fact that more than one half of the lesions in this group were within the mouth, and that in the male syphilis, bad teeth and smoking are more common than in the female.

Etiology was studied in the nineteen cases. In five males and three females there was nothing that would suggest the cause of the disease. In one male and two females there was a possibility of irritation from a dental plate. Trauma was mentioned in the cases of one male and two females. The use of tobacco and the presence of bad teeth were listed in three males. In one female no history on this point was recorded, and in one male a supposed sebaceous cyst had been removed from the nasal end of the lacrimal duct. Thus one can find no definite causal agents for this group of tumors. Cohnheim's theory of embryonal rests, or bits of misplaced tissue, must suffice until further information is elicited.

Occupation and nativity seem to have no bearing on the disease.

Ulceration was definitely present in nine and absent in four of the patients. In six cases there was no definite statement, but five of these probably had ulceration. It was difficult to tell whether or not the ulceration was spontaneous. Many of the patients had had treatments before coming to the Memorial Hospital.

In none of the cases was there any familial history. There was no tendency for any of the lesions to remain stationary or to involute without treatment.

In only four cases was there any definite history of bleeding before treatment. These patients either had a primary lesion of the nose or an extension into that organ.

The detection of a swelling by fifteen of the patients caused them to seek medical advice. One swelling was first detected by a dentist who was caring for the teeth.

In seven of the cases there was localized pain of a steady, dull type. Soreness was complained of by one patient who had a lesion of the mouth and by another who had a swelling of the tongue.

There were no definite preexisting lesions.

As nearly as could be determined, the palate was the primary site in seven of the cases, the antrum in three, the mucosa of the cheek in two, the alveolar ridge in three, the lip in one, the tongue in one and the nose in two.

The disease progressed by direct extension. Those lesions primary in the palate usually entered the nose and antrum. The ones which began in the nose and antrum ordinarily invaded the mouth, orbit and ethmoids. In at least one case the meninges were involved by direct extension into the cranial cavity. The anatomic relations of the parts usually affected make this method of spreading easy and render the tumor dangerous.

In most of the cases there are no data concerning the duration of the lesion before the patients came to the Memorial Hospital.

Fourteen cases have been observed for three years or more, and these are the only ones that will be used in the follow-up study.

Previous treatment consisted of surgical excision in the majority of the cases and irradiation in a few. From this it would seem that the medical profession in general is not aware of the beneficial results that may be obtained from a well executed plan of irradiation therapy. When employed, this treatment should be given as early as possible. This form of treatment is recommended because of the relative radio-sensitivity of this group of tumors and on account of the discouraging results obtained from straight surgical measures.

The treatment at the Memorial Hospital consisted of irradiation primarily and surgical intervention secondarily. External applications

(usually radium rather than roentgen ray) were employed in twelve cases. As a general rule, the radium was applied locally over the area of involvement, and if the neck was irradiated, it was customary to utilize the roentgen ray. At the present time, however, there is an increasing use of large radium packs both locally and to the neck. By means of isolated clinical observations it has been thought that this method can be supplemented with the high voltage roentgen ray, thereby giving a larger tumor dose with less injury to the skin than can be given by either form of irradiation separately. It is hoped that results will be improved by this method.

Interstitial irradiation, which usually consisted of radon enclosed in glass tubes (for about the past four years gold tubes have been used), was resorted to in all but three cases. In one of these three the lesion was in the lower lip and could be effectively treated by external irradiation alone. In the other two, the disease was so far out of bounds and was progressing so rapidly that strenuous measures were not deemed justifiable.

Surgical intervention was employed in seven of the fourteen cases. In five of these it consisted in evacuation of the orbit or antrum, sometimes one and at other times both, in order to remove infected or overirradiated tissue. The overirradiation was purposely planned, the neoplasm being used as a radium holder, with the expectation of removing the tumor tissue before it necrosed or became infected. In the case in which there was a lesion on the lip, local excision was sufficient. A submaxillary dissection was performed in the case in which there was a neoplasm of the mucosa of the cheek. The extirpated tissue was negative for tumor growth.

Results show that of the fourteen patients observed for three years or more, five were lost trace of. Of these five, one was followed-up for too short a time to predict permanent results. This was the patient with the lesion on the lip and when last seen there was no evidence of disease. One (primary tumor of the palate) is probably dead. The remaining three patients were followed-up for three and one-half, three and two years, respectively. At the end of this time they were all free from disease and in such excellent condition that one might assume that they are still alive and well. Two of these had primary tumors of the palate, and one had a neoplasm arising from within the nose.

Only two of the patients are definitely known to be alive. One of these, who has been followed-up for four years, had a primary tumor in the mucosa of the cheek. In the group of squamous carcinomas, this site would be regarded with unusual apprehension, for metastases would be expected. When the patient was first seen the lesion was very extensive and despite previous excision had infiltrated the masseter muscle. The treatment at the Memorial Hospital consisted in cautery

excision of the ulcerating lesion and the application of external and interstitial irradiation. The second patient, who has been followed-up for six and one-half years, exhibited an ulcerating lesion of the soft palate measuring about 3 cm across. The therapy consisted solely in one insertion of bare tubes into the lesion.

Seven patients are known to have died. Three had primary lesions in the palate, three had lesions originating in the maxillary sinus, and one had a lesion arising from within the nose. The high mortality may be explained by the fact that the patients came late, and the disease was so extensive that there was little hope of even slight palliation. In some, if not all, it seemed that previous ineffective treatment had aggravated the condition.

The duration of treatment and the duration of observation were so often terminated by the death of the patient that no definite conclusions could be drawn from such a study.

Complications were frequent and often severe. In the late stages pain, insomnia, anorexia and asthenia were common. Sequestrums were noted in at least two cases. Infection was frequently the immediate cause of death. In three cases there were signs and symptoms of infection of the central nervous system (meningitis or brain abscess). One patient had acute parotitis.

Conceding that minor histologic differences could be seen in some of the tumor tissue, this feature did not seem sufficiently marked to account for the difference in the mortality.

*Mixed Squamous and Adenoid Cystic Basal Cell Carcinomas From Noncutaneous Sites*—In addition to the foregoing nineteen cases there were two that combined a few squamous with the adenoid cystic features. One of the patients had a primary tumor of the palate which apparently developed some squamous characteristics during the course of treatment at the Memorial Hospital. She was under observation for seven years, and there was evidence of local disease at the time of death. Physical signs were suggestive for fluid in the pleural cavity, but autopsy was not performed. The second patient, who had a primary lesion in the nose, has been followed up for eight years, and he seems free from disease. There were several recurrences, all of which yielded promptly to treatment.

#### HISTOLOGY

The material from the Memorial Hospital consists principally of small pieces of tissue, as is usually taken from biopsies, and, therefore no gross descriptions can be given. It is believed, however, that macroscopic features are not as important as the clinical observations and consequently would add little of value to what has already been given.

The histologic difference between the *cutaneous* and the *noncutaneous* basal cell tumors in this series is sometimes slight and can be given briefly, otherwise, a single description will suffice for both kinds

In the tumor found in or near the skin, more of the typical basal cell characteristics are seen, and the surrounding connective tissue is more prominent. In the collection from the Memorial Hospital there are sections that demonstrate the origin from the basal layer of the epidermis, but there are two cases which are likewise observed to be springing from the analogous tissue of the oral mucous membrane. In

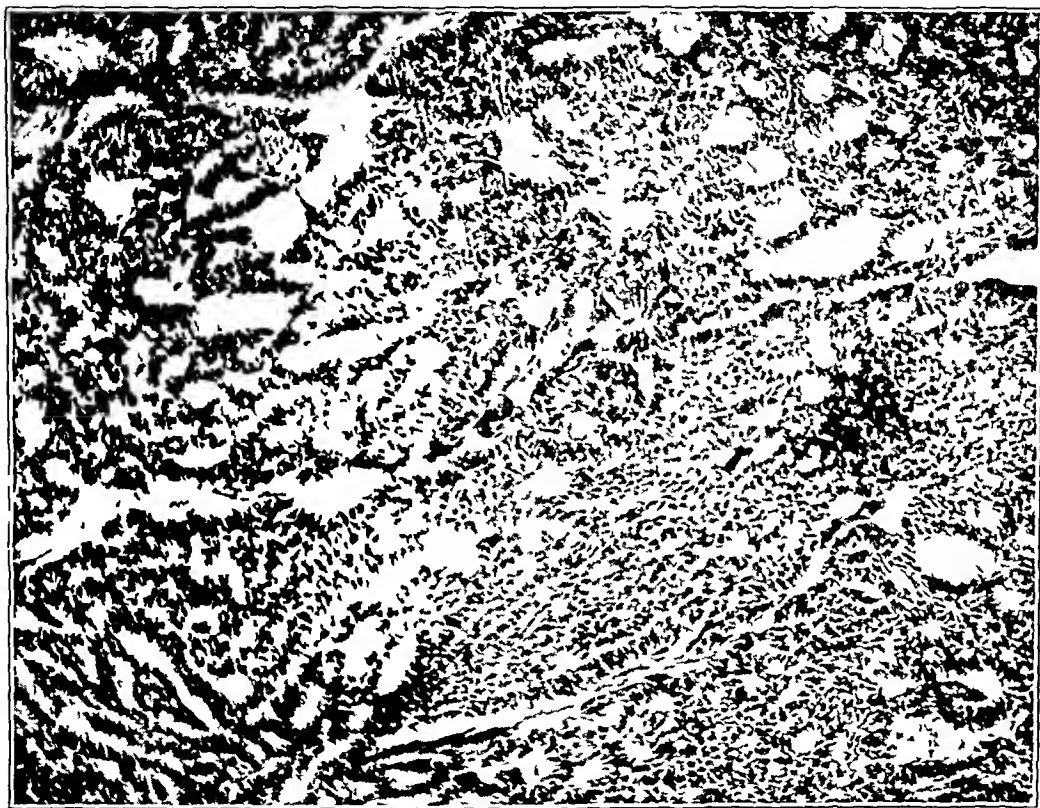


Fig 1 (cutaneous group) —Primary lesion in the upper eyelid, which had existed for eight years, with a slow, progressive growth. After treatment began the patient had recurrences for two years. For the past five years the patient had been free from disease. The structure is typical for low power.

two of the cutaneous tumors there is distinct production of cartilage, and in other respects these two present the picture of the so-called salivary gland type.

Henceforth, the description applies to both the cutaneous and the noncutaneous types.

Under low power magnification, the tumor cells may be seen in large compact masses, broad sheets, small clumps and strands of varying size or as loosely scattered individual cells. Any of these forms may



exhibit infiltration into the surrounding tissue. The cells on the periphery (more marked in larger masses) often present a palisade arrangement.

Within the tumor cell nest may be observed cysts of varying size and poorly developed adenoid structures (not seen in many), and it is not uncommon to find the cells arranged in a finely interwoven, lacy network. Many of the cystic areas are empty, others are occupied by a smooth, homogeneous substance, these areas are usually contracted,

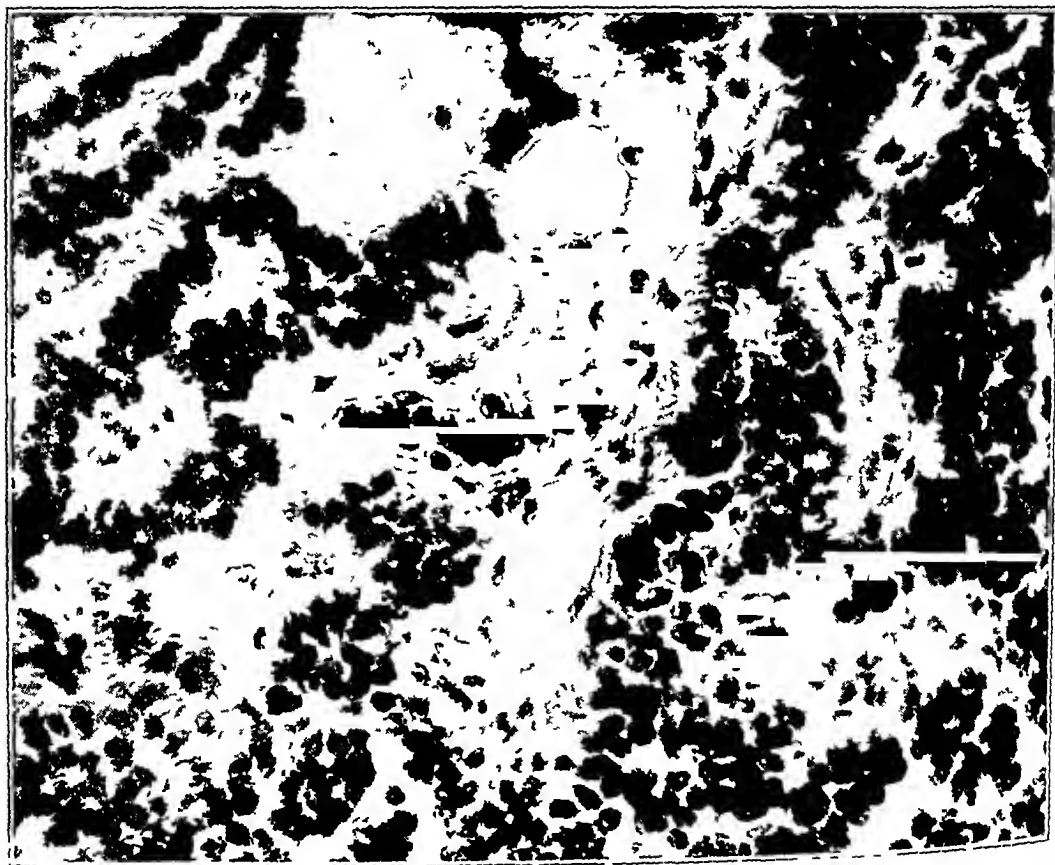


Fig 2 (cutaneous group) —The patient had a twenty years' history of a small lesion of the skin of the face adjacent to the nose. There was no recurrence during the one year of follow-up study. The same cell type but different arrangement is seen as in the metastases from fatal cases in figures 6 and 9.

leaving a free area adjacent to the tumor cells, and may be due to fixation. The neoplastic cells are moderately hyperchromatic.

Under high power magnification the palisade-like cells often noted on the periphery are clearly seen to be pointing toward the center, where they are closely packed and narrower than elsewhere. The cytoplasm is scanty and is frequently absent. In contradistinction to its appearance under low power, the nucleus now shows clear areas with many uniformly distributed granules of varying size. In some

areas there is a meshy network seen connecting the larger granules. Nucleoli are rare, and mitoses are infrequent. Many of the cells are undergoing dissolution. Ordinarily this process becomes more marked as one leaves the periphery and goes toward the center. At times only a portion of the nucleus can be seen, in some all has disappeared except the nuclear rim. In those cases in which disintegration is complete, or nearly so, the granules that had been in the nucleus may be easily detected lying between cells which are still intact. This tendency toward dissolution can be found in individual cells, but the more striking

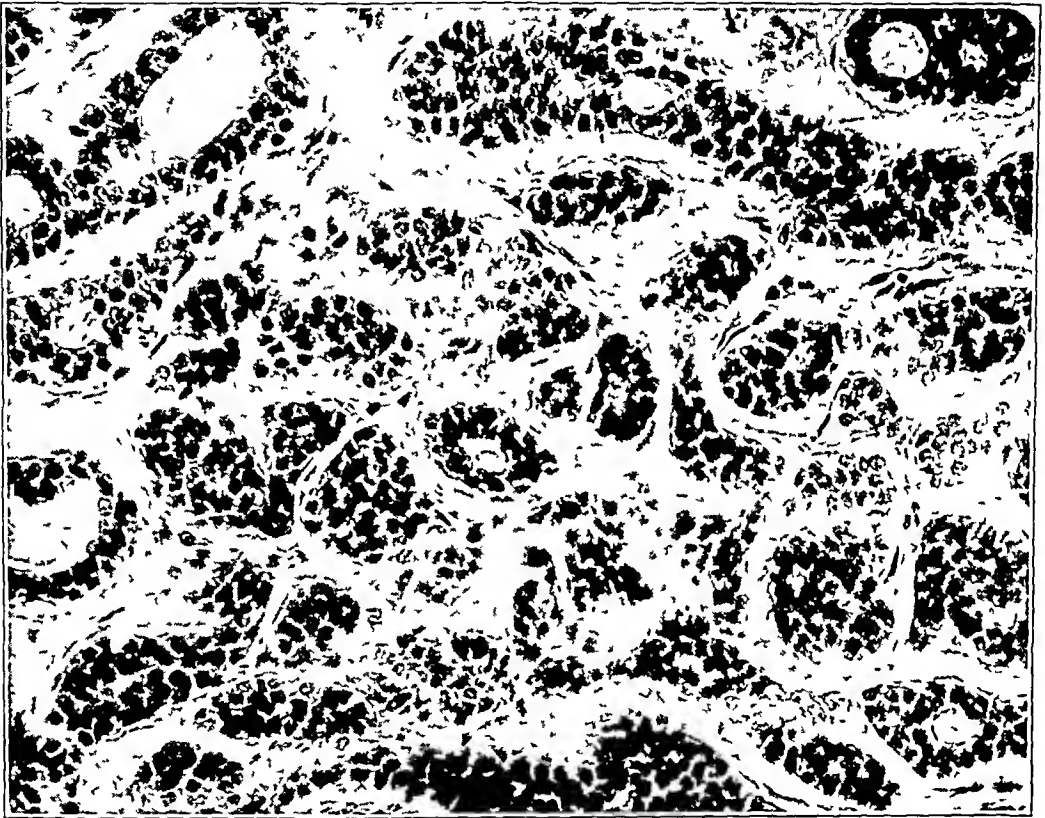


Fig 3 (noncutaneous group) —Small lump in the soft palate noticed for four months. Regression was complete. The patient was followed-up for six and a half years. The central adenoid spaces are well marked.

examples are those in which small clusters seem to participate simultaneously in the process. In the latter instance the cystic areas are formed, and in the former a granular stroma is seen with here and there the absence of one or more cells.

When the cysts are thus formed, they seem to enlarge progressively by the continuous dissolution of the marginal cells. Thus these centers may become as yawning caverns continually advancing at the expense of the neoplasms. This process becomes an attack from within and

one may wonder whether at times the rate of central destruction may thus equal that of peripheral growth. The enlarging cysts may meet others and coalesce with them.

It is easy to conceive that the contents of the cyst may be made up of cellular remnants and debris. Ordinarily this appears as a granular coagulum with occasional interlacing fibrils. In this structure, somewhat as a matrix, there may be embedded portions of partially destroyed tumor cells. Thus it will be seen that what usually appeared as a homo-

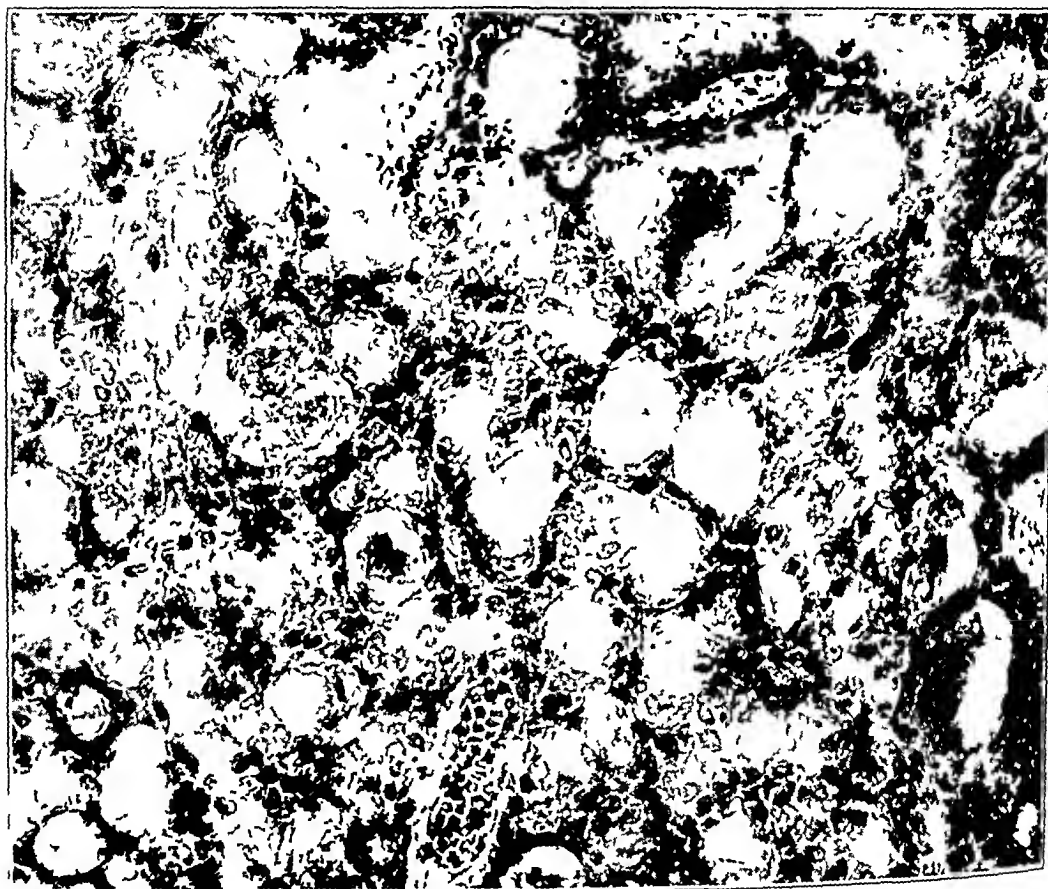


Fig 4 (noncutaneous group) —The lesion apparently originated in the antrum. Four years' history of epistaxis. The patient died five months after admission with symptoms of meningitis. Autopsy was not performed. The patient probably had an extension backward. The lacy-like network is prominent.

geneous mucoid substance under low magnification may transform itself under high power into a graveyard littered with remains of dead neoplastic elements.

In a few instances the cysts contain a definite hyalinized material resembling that often seen in squamous epithelium. Also it is possible to find areas of connective tissue circumscribed by epithelial tumor cells and in such cases they appear as cystic structures containing connective tissue. These might be termed pseudocysts.

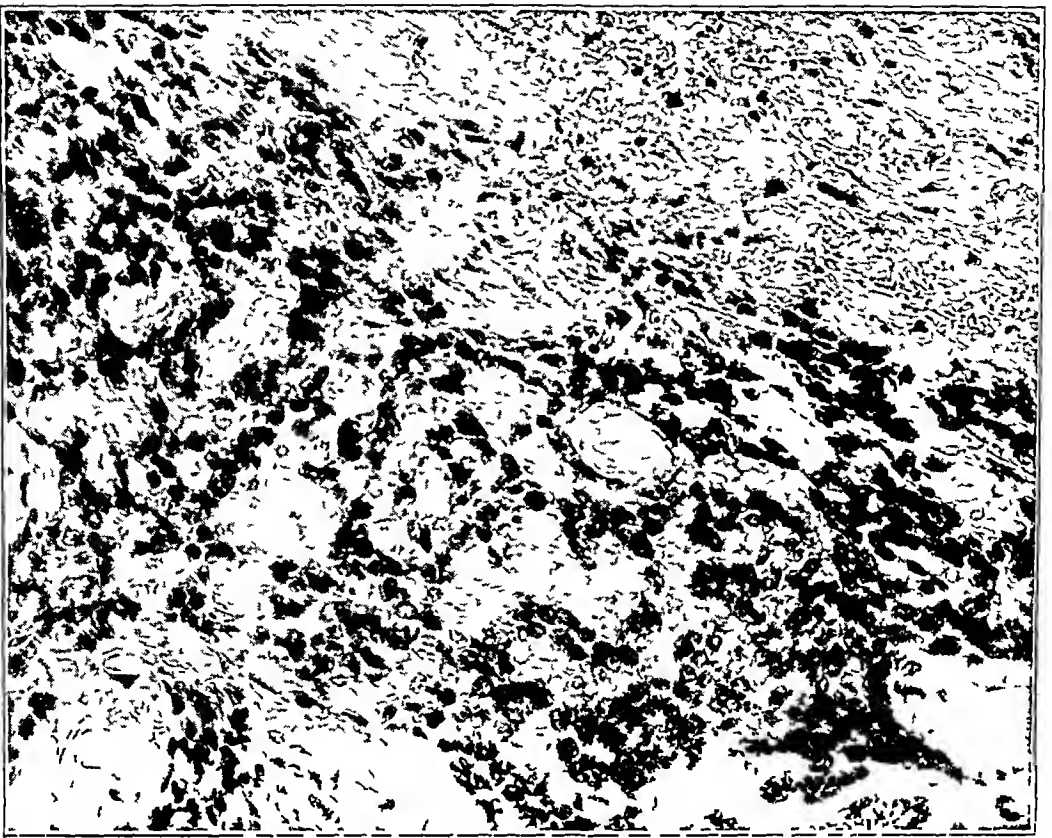


Fig 5 (case 1) —(Cases with generalized metastases) The primary tumor of skin near the nose The enclosure of connective tissue by tumor cells, forming cystlike areas, is demonstrated

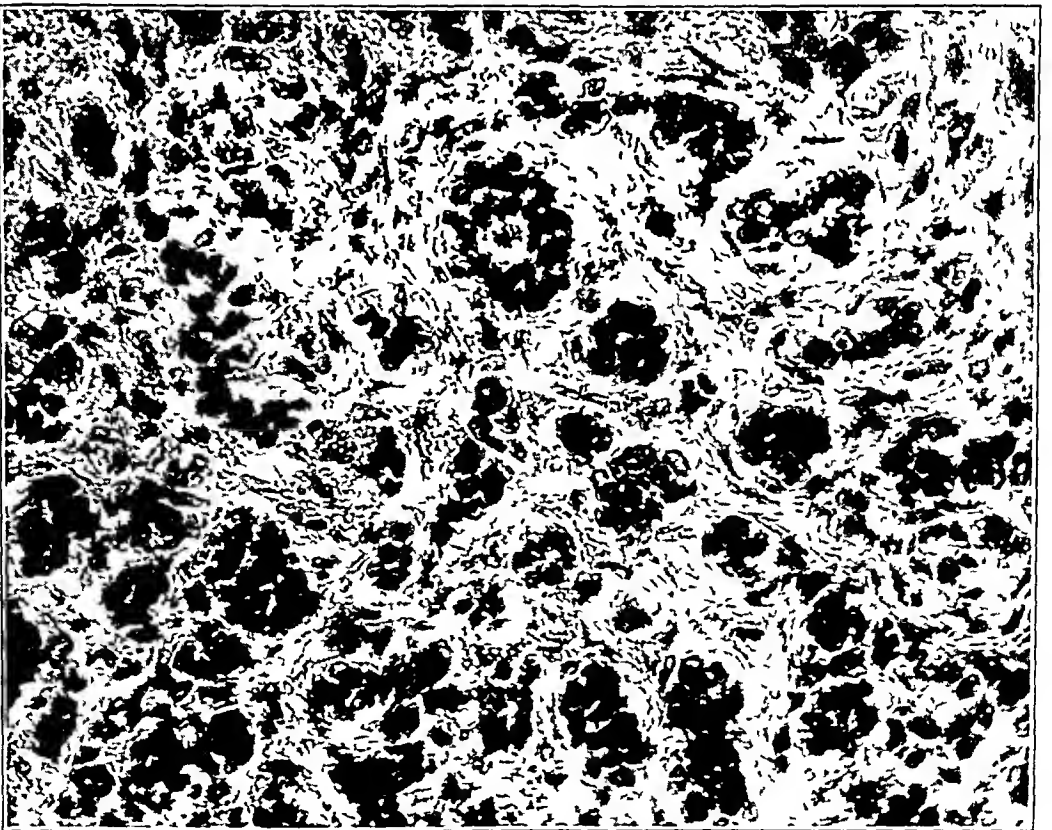


Fig 6 (case 1) —(Cases with generalized metastases) This shows the metastasis to the spleen The cells have changed character somewhat but are definitely of the same type, as in figure 5 Cystic areas are not numerous but may be round

It is not difficult to find some tumors in which the spaces are occupied by a bluish-white substance. In most of these the cysts are poorly formed. It is reasonable to suppose that such a picture could result from the juncture of two or more strands of tumor cells which had thus snared off a bit of connective tissue, and that the subsequent degeneration of the connective tissue could produce a substance resembling mucus. It is doubtful if the cystlike areas contain a true mucoid substance. As far as one is able to determine with the microscope, it would seem that the intracystic material is a product of cellular degener-

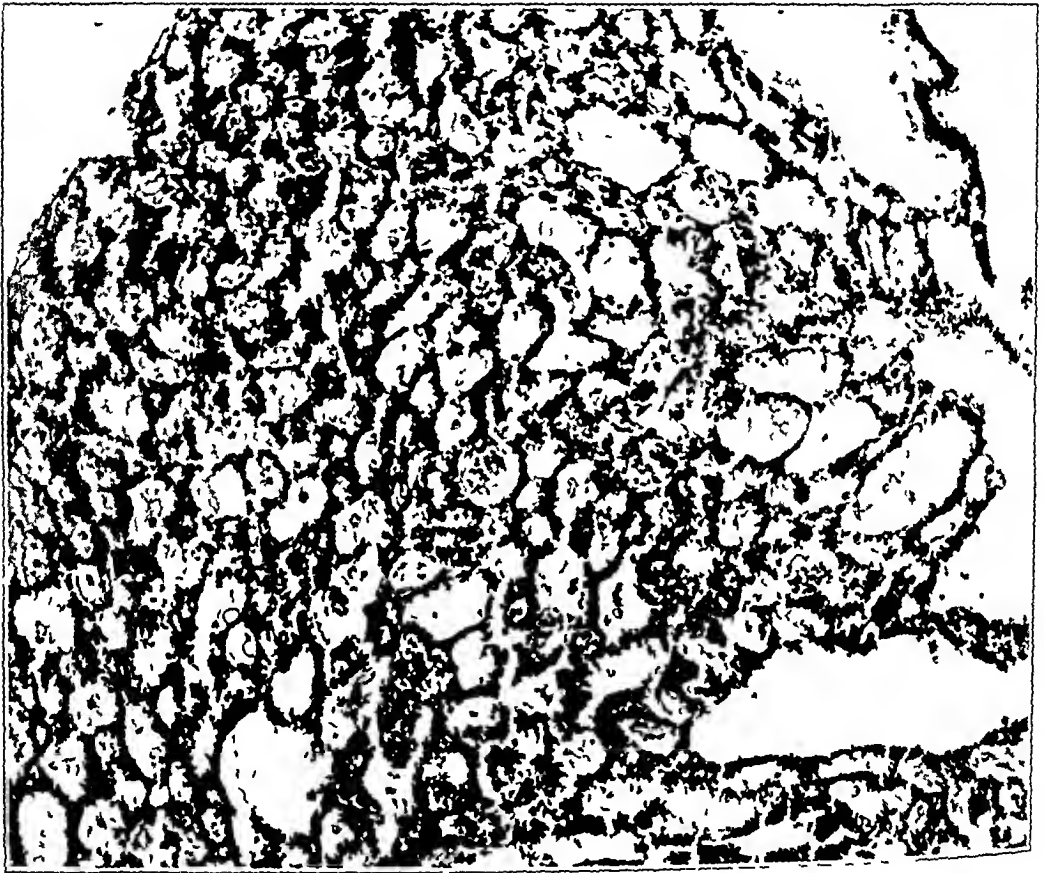


Fig 7 (case 2) —(Cases with generalized metastases) The primary (very old section) tumor of the submaxillary area. Note the resemblance to thyroid or to pulmonary tissue seen under low power.

ation rather than of secretion. However, through the kindness of Dr Alfred Plaut of the Woman's Hospital (New York) I have been able to study the mucicarmine reaction in two cases, premenstrual endometrial tissue being used for a control. The staining reaction thus employed was positive in the adenoid cystic tumors, but it is doubtful if the test is specific enough to differentiate between mucus resulting from cellular activity and colloid material coming from tissue degeneration. For the present it seems wise to leave this point unsettled.

In some tumors there are well formed cysts which may exhibit a distinct membrane. How the latter structure is formed is not definitely determined. The contents of the cysts may have produced it by pressure, the force thus exerted being sufficient to cause condensation of intercellular material. Possibly the action of chemicals in the fixatives and stains may have something to do with it. One cannot say.

In general, the adenoid structures are poorly developed, and one often has to imagine them. In a few sections, however, they seem fairly definite and possess not only an internal but also an external

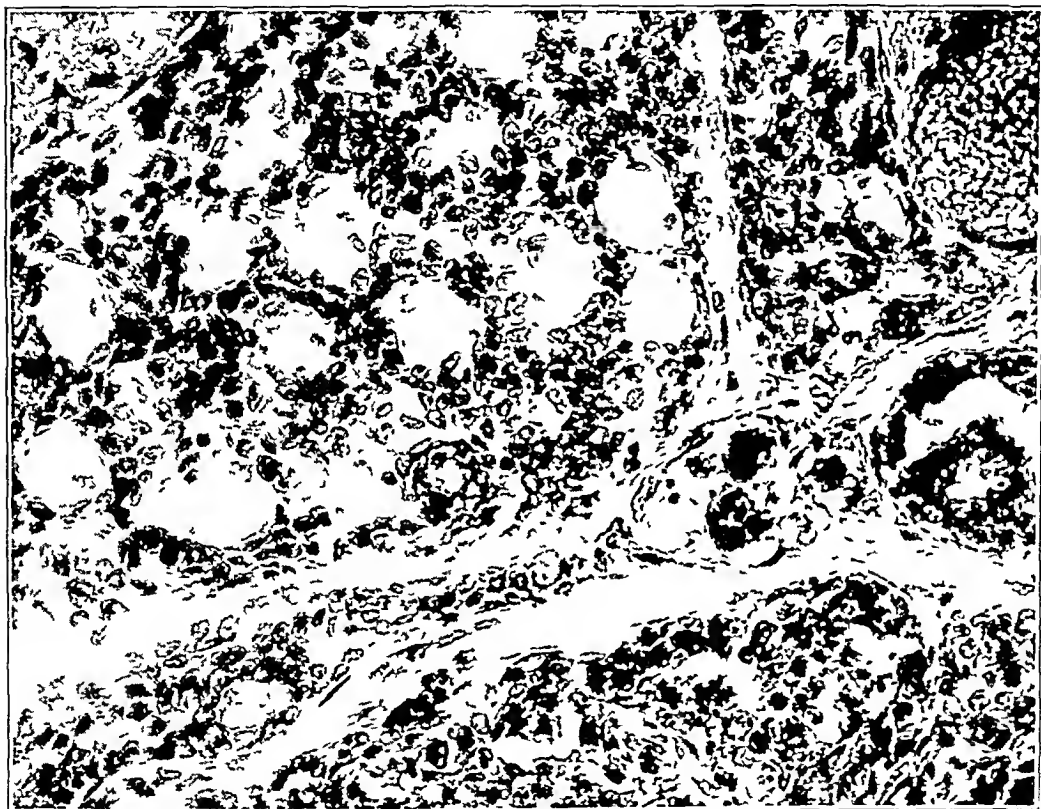


Fig 8 (case 2) — (Cases with generalized metastases) The metastasis in the lung from the primary tumor represented in figure 7. The character of the cells has been retained.

limiting membrane, each of which is well formed. But even here the described unit often appears much more like a tubule or duct than a gland proper. In some sections I must confess that I have found the adenoid structures wholly lacking, or else of an indefinite character.

Typically, the stroma is very scanty. A few fibrils with some loose granular bodies may be scattered between the tumor cells. Since most of this is probably a degeneration product of the tumor cells themselves, one can assume that such a structure is hardly comparable to a true stroma. In some instances there is some supporting connective tissue of



the usual sort, but as a rule this is really extraneous and has been infiltrated by tumor cells. In only a very few places is it possible for one to see a fine, closely packed connective tissue which seems to act in the nature of a capsule. The connective tissue seems to be destroyed by the liquefactive properties of the tumor.

Aside from the cartilage formation mentioned, there may be other noteworthy structures. In two sections there have been observed many small, closely packed blood vessels which occupy a considerable portion of the tumor tissue. In these the actively growing neoplastic cells seem



Fig 9 (case 3) —(Cases with generalized metastases) The metastatic lesion in the liver. Central degeneration has begun, showing one method by which the cysts are produced. The primary tumor was reported as adenoid cystic epithelioma by a competent pathologist. Some of the general features have undoubtedly changed, but the individual cells are typical and resemble those in figures 2 and 6.

to be infiltrating the walls. They are not altogether typical, however, and it may be that the proliferating cells are from the blood vessels, in which case one may presume that one is dealing with a mixed tumor, an angio-epithelioma, if there is such a tumor. In one section there appears to be hyperplasia of the mucous glands, but this process probably represents an excitation due to the invasion by tumor cells rather than a true neoplastic response.

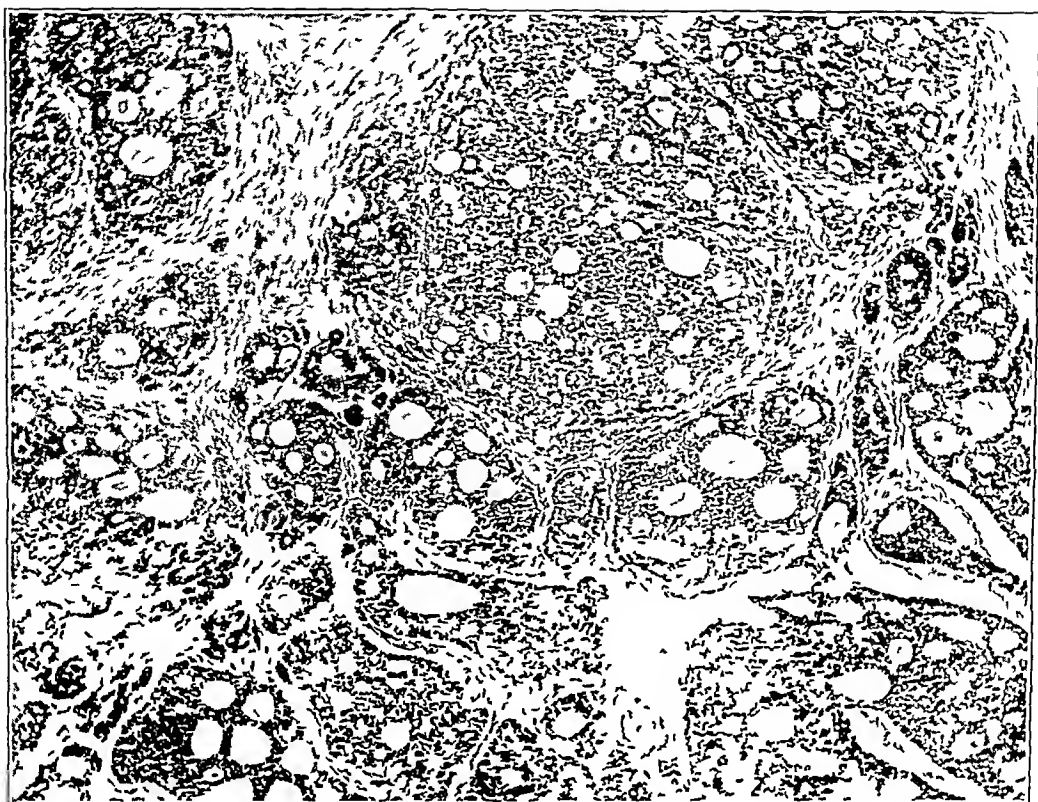


Fig 10—Recurrent nasal tumor, generalized metastases This illustrates the well marked cystic areas and the general character of the neoplasm

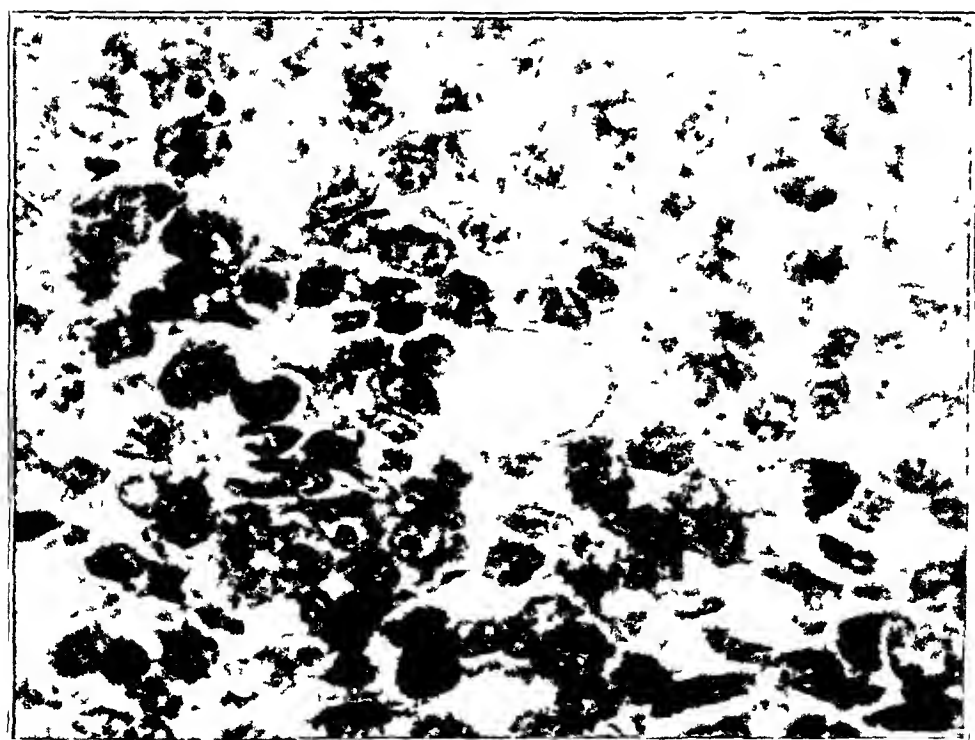


Fig 11—A cellular area of figure 10  $\times 1,300$  An early stage of cyst formation and some well preserved cells are depicted



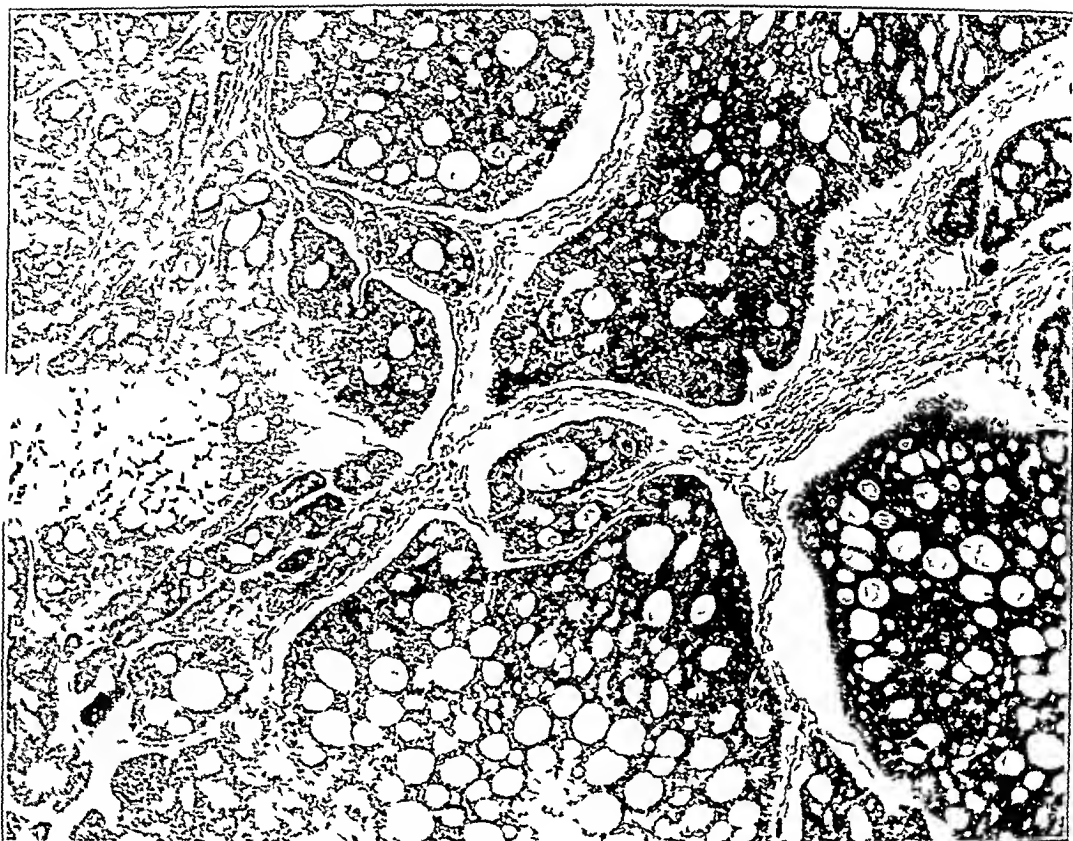


Fig 12—Metastatic nodule in the omentum,  $\times 85$  The structure is identical with that in figure 10

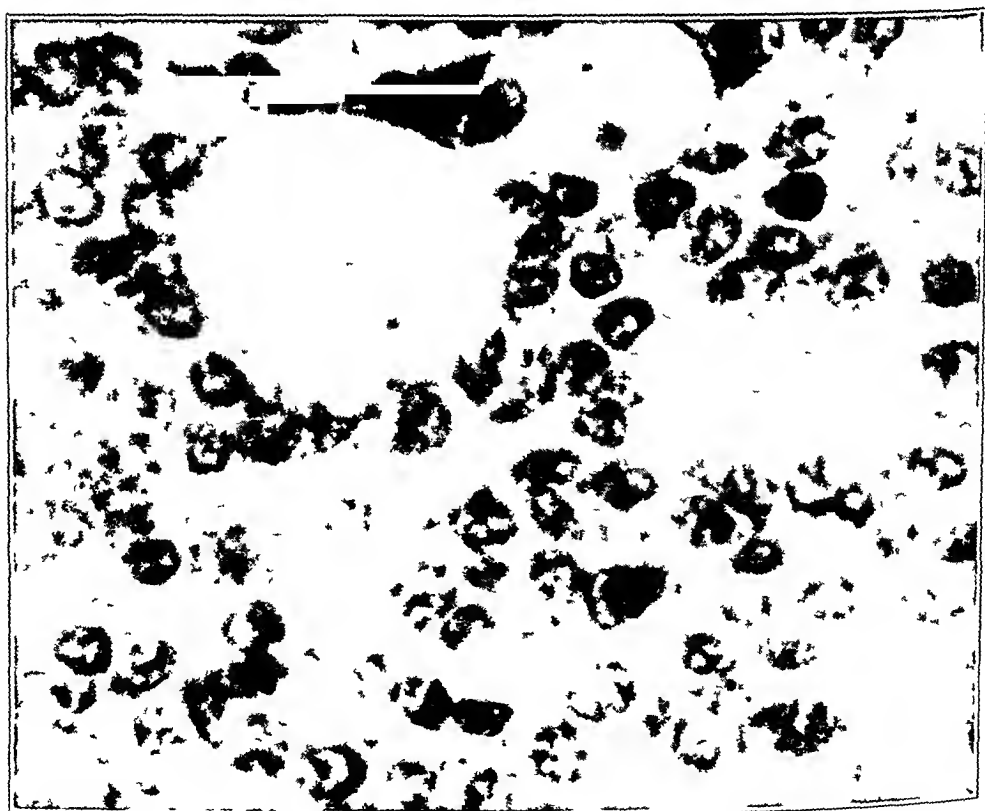


Fig 13—A cellular area of figure 12,  $\times 1,300$  The degeneration of cells which seems to precede the formation of the cysts, may be seen

## SUMMARY

In both the *cutaneous* and the *noncutaneous* groups the age of appearance of the lesions, the lack of familial qualities, the tendency to progression without limit and usual presence of ulceration all dispose one to believe that the cases of adenoid cystic carcinoma analyzed should not be classed with the relatively benign skin disorder known as adenoid cystic epithelioma or as Brook's disease. These cases are more closely related to the usual type of basal cell carcinoma (Krompecher), but many do exhibit adenoid and cystic features.

The study of etiology was interesting and slightly suggestive but nothing more. Sex, occupation and nativity seemed to have little if any bearing on the disease.

The *cutaneous* lesions were situated for the most part on or near the nose or eyelids, while the palate was the most common site for the *noncutaneous* tumors. In the former it was usually the presence of ulceration, and in the latter it was tumefaction, that caused the patient to seek medical advice. The average duration of the skin lesions before the person came to the Memorial Hospital was seven and one-half years. It was impossible to determine accurately this point in the other group.

In the follow-up study, no case was used unless it had been observed for at least three years.

In the *cutaneous* group, fifteen patients were found suitable for such study, twelve had had previous treatment. The treatment usually consisted of the application of salves, but in some cases both surgical intervention and irradiation had been employed either separately or together. Only one patient is known to have died, and the case was obviously hopeless from the start. Recurrences and complications were frequent, but apparently the disease was finally controlled. The average duration of treatment was slightly more than two years.

Mixed basal and squamous carcinomas were found in both cutaneous and noncutaneous groups, but the number of cases was too small to afford more than passing comment. It would seem that the addition of squamous features gives a poorer prognosis.

In the *noncutaneous* group, fourteen cases could be traced for three years or more. In these cases the previous treatment had usually been surgical intervention. At the Memorial Hospital this procedure was used as an adjunct to irradiation. In many of the cases palliation was all that could be expected. The mortality rate proved to be about 50 per cent. The complications were numerous and severe.

I believe that the great difference in mortality between the two groups cannot be explained on the basis of histology but rather on the fact that in the noncutaneous type the anatomic setting facilitated the

direct extension of the disease into the accessory nasal sinuses and thence even into the cranial cavity. Infection as well as tumor can proceed by the same route and thus dispose of the patient.

Adenoid cystic basal carcinomas are ordinarily radiosensitive, and, as a general rule, the patients should be treated by irradiation (preferably radium) primarily and surgical intervention secondarily.

The histology of these tumors is extremely interesting. The term adenoid cystic carcinoma is explanatory. Many cases lack the glandular features, and in some the cysts are poorly developed. The supporting structure is composed of connective tissue, and in some instances it may contain a substance resembling mucus. The intracystic material is probably the remains of degenerated neoplastic cells and is not a true secretion. The mucicarmine reaction was positive in the only two cases in which it was employed, but it is not believed that it is necessarily specific for mucin.

#### REPORT OF CASES

There were three cases in which generalized metastases were found. These cases had no squamous features, and their unusual course warrants separate, detailed reports, therefore, they were not included in the foregoing cases. I believe that such widespread dissemination of a basal cell carcinoma has not been reported before, or if so I have not found an account of such. The fact that a basal cell carcinoma may metastasize is given little thought by most physicians, and, although such an extension is rare, one should keep in mind the potential danger of these tumors. In the "adenoid cystic" subdivision of basal cell carcinoma, the possibility of generalized metastases should not be forgotten. It is hoped that the following case reports will justify this statement.

CASE 1—*History*—A white man, a clergyman, in 1917, at the age of 58, noticed a "spot" 2 mm in diameter on the cheek near the right nasolabial fold. It looked like a bit of black dust, was crusted and would not heal. Several months later the lesion was treated with radium. Apparently the lesion disappeared, only to recur two years later, when it was again subjected to an application of radium. The regression was not as satisfactory as on the first occasion. The following year the area was excised and skin grafted. The diagnosis by a competent pathologist was basal cell epithelioma of the face. Three months later a recurrence in the scar was excised.

Following this treatment the patient had four other excisions for recurrences. Each time the diagnosis of basal cell carcinoma was returned. He also received five applications of radium on the edges. Injections of an unknown calcium preparation were given.

Although in 1920 he was treated twice for recurrences in the outpatient department his first admission to the Memorial Hospital was on July 7, 1927. He stated that for the past five months prior to admission he had had generalized subacute pain in the sternum and ribs. The distress was accentuated by breathing deeply. Three months before admission he had a pathologic frac-

ture of the right clavicle. Several weeks before coming to the Memorial Hospital he was comatose, but recovered fully and promptly. In at least two other institutions of highest rank (in one of which he had been previously treated) the diagnosis of multiple myeloma was made from x-ray pictures. The roentgenograms confirmed the finding of destruction of bone in the spine, ribs, skull, pelvis and other bones. Despite some atypical features in the x-ray films and disregarding the existence of a previous basal cell carcinoma, because they were not thought to metastasize, the provisional diagnosis of multiple myeloma of the bones seemed justified.

*Physical Examination*—The patient was well developed and nourished, and intelligent, alert and responsive. The right alar nasi was absent. There was a slight ulceration of the nasal lesion, and the edges were somewhat raised. The lesion appeared to be an unhealed benign process rather than a recurrent epithelioma. Otherwise, the nose was normal. There was a slight protuberance over the right ninth rib anteriorly. The abdomen was soft but slightly distended. The urine occasionally revealed hyaline and granular casts. Examination for Bence-Jones bodies gave negative results. The blood count varied from a hemoglobin of 90 per cent with 4,200,000 red cells on admission to a hemoglobin of 50 per cent with 2,500,000 red cells about two months afterward. Calcium was 15.8 mg per hundred cubic centimeters of blood. Nucleated red blood cells (one to five) were found in four of the eleven examinations.

*Treatment*—(1) A moderate amount of external irradiation with the 4 Gm radium pick and the high voltage roentgenray was given over the chest and back. (2) A glass hull (ridon) was applied once to the nose. (3) Ultraviolet light was applied on the trunk.

*General Course*—While the patient was in the hospital, the general course was slow and progressively downward, characterized by anorexia, malnutrition, mild rise in temperature, slight elevation of pulse rate and gradual diminution in mental power. The patient died on Jan 5, 1928, at the age of 68, the disease having lasted ten years.

*Autopsy*—Marked emaciation was evident. The right alar nasi was missing; the ulcerating tissue appeared neoplastic. There was a marked, lateral, thoracic scoliosis of the right side. There were many rounded tumor nodules in the ribs. Extensive adhesive pleurisy was present on the left side and slight on the right. The heart was small, the muscle was brown, and the right side was distended. The right lung was emphysematous, with a few indurated bronchial thickenings, both lungs suggested neoplastic involvement. The spleen was dotted with milium nodules. The liver was normal in size, with small nodosities on the superior surface, of the right lobe. The kidneys were small, the capsule was stripped, leaving a granular surface, the cortex was thin. There were numerous adhesions from the omentum to the peritoneum, one of which produced some constriction of the cecum. The urinary bladder was distended with cloudy, purulent looking fluid. The prostate was small and normal. There were calcific deposits in the dura mater, there was edema of the pia mater, and the brain and hypophysis were normal. The skull was honeycombed with numerous fatty-like, partially calcified areas. It was much enlarged and thickened. The same process appeared in the ribs, clavicles, pelvic bones and femora.

*Diagnosis*—The anatomic diagnosis (microscopic) was (1) adenoid cystic basal cell carcinoma arising from the skin of the right cheek, extending into the nose and metastasizing to the dura mater, lungs, spleen, liver and various bones (notably the skull), (2) chronic arterial nephritis, adhesive pleurisy.

*CASE 2—History*—The patient was an elderly, white, business man, whose exact age does not appear on the record and who gave no history previous to Nov 13, 1911. At that time he had a localized, easily shelled out tumor. It was situated near to but was separate from the left submaxillary salivary gland (report from attending surgeon). It seemed to be lying in the subcutaneous tissue. Pathologic examination revealed adenoma with probably commencing cancer.

*Treatment*—On July 21, 1913, there were one nodule, the size of a filbert, at the upper part of the old incision, several metastases in the fat tissue and an infiltrating mass extending beneath the mylohyoid muscle backward beneath the great vessels, involving these and the adjacent muscle. The facial artery was thickened. The hypoglossal and glossopharyngeal nerves were saved with difficulty, the branch of the facial nerve going to the mouth was sacrificed. The dissection extended down to the cricoid cartilage (where a soft gland was found) and to the constrictors of the pharynx. The procedure was radical and complete. By pathologic examination, the cells seemed typical of endothelial rather than of epithelial origin. The tumor was pronounced malignant.

During the winter of 1913, the patient froze his face and had considerable irritation of the skin. In May, 1914, one gland was found in the submental triangle and another in the submaxillary space. A thorough dissection was performed. Pathologic examination showed normal lymphoid structure with fat and fibrous tissue, but no new growth.

On Jan 16, 1916, a fourth operation was performed for recurrence beneath the jaw and another lesion over the lower border of the jaw, external to the mandible. The largest gland was 1 cm in diameter. Complete dissection was carried out. The tonsils were enlarged so that a tonsillectomy was performed. Gross pathologic examination revealed the tissue from the neck was 5 by 4 by 2 cm, in which there was a dense nodule 1 cm in diameter. Microscopic examination revealed tubular glandular tissue, and one place infiltrated into the connective tissue. The diagnosis was adenocarcinoma. The rest of the tissue was normal. The tonsils were large but normal with few enlarged crypts.

On June 5, a nodule (just above the hyoid bone) and the digastric muscle were removed, together with the two small nodules along the hypoglossal nerve, which was then sacrificed. Pathologic examination showed a piece of tissue, the size of the little finger in the midst of which there was a dense infiltrating growth composed of large plexiform masses of small, undifferentiated epithelial cells with a marked tendency to degeneration, forming small ringlike openings. Masses of cells were separated by trabeculae of connective tissue. There were also small solid masses in the adjacent fibrous muscular tissue. The diagnosis was carcinoma not classified.

The patient was treated by the staff of the Memorial Hospital from Oct 30, 1920, to March 7, 1926. When first seen, he had a nodule in front of the left mastoid process, and there was some bulging in the left tonsillar fossa.

He received seventeen treatments with radium, distributed as follows: neck (four), submaxillary area (four), spine (seven) and chest (two). All of the treatments were external except three to the submaxillary space, which were interstitial. Palliation was slight, and the patient died on March 13, 1926, fifteen years after the first operation.

*Autopsy*—The patient was well developed and nourished. Below the left side of the jaw there was a depressed area of scar tissue 10 cm long, slightly adherent to the mandible. The skin was leathery and the buccal mucous membrane was intact. There were no gross signs of tumor on section. The left tonsillar region was the seat of a firm, leathery, cicatricial mass, 4 cm in diam-

etc., movable on the deep tissue and adherent to the intact mucosa. There were several minute cysts filled with mucus and some calcific points. No definite tumor was visible. At the level of the base of the tongue was a third mass, 2 cm across. It was hard and contained many cysts, considerable opaque tumor tissue and numerous blood sinuses. The heart was large, but was otherwise normal. In the visceral pericardium there was a fibrous plaque 3 cm across. Two hundred centimeters of straw-colored fluid was found in the pleural cavities. The pleurae showed a dense generalized fibrous thickening, and they were the site of flat, cicatrized, centrally depressed tumor masses, averaging from 1 to 3 mm in diameter. In the lungs were numerous tumor nodules, from 0.5 to 2 cm in diameter. Some tumor masses appeared densely fibrosed, while others were soft. There was no enlargement of the lymph nodes, congestion or pneumonia. The spleen was slightly enlarged, the follicles were invisible. The liver was of normal size with a few miliumary tumor nodules. The suprarenals, stomach, pancreas, bladder and prostate were normal. In the spine there was a slight sharp kyphosis of the fourth and fifth lumbar vertebrae. The right transverse process of the fourth lumbar vertebra was enlarged and the periosteum was thickened. The body of the sacrum, all of the lumbar, the eleventh and the twelfth dorsal vertebrae cut readily with a knife. The osseous tissue was congested and mottled throughout by opaque tumor areas. The remaining bones were not examined.

*Diagnosis*—The anatomic diagnosis (microscopic) was recurrent carcinoma, originating in the left submaxillary space, extension to the left tonsil and base of the tongue, metastases to the lungs, pleurae, liver and spinal column.

*Comment*—In the scar tissue below the left side of the jaw were scanty tumor cells which were atrophic and degenerated. The tonsillar mass showed fibrosis and calcification. On the lower edge there were isolated foci of tumor cells which contained widely dilated blood sinuses. In the intermediate nodule at the base of the tongue there was well preserved tumor tissue with many small mucous cysts. The lungs exhibited diffuse fibrosis and degeneration of the tumor cells together with some foci of the large cells with hyperchromatic nuclei. The liver presented active proliferation of the tumor cells, and in the spinal tissue there was alveolar and diffuse carcinoma. Some of the bone-marrow showed a peculiar necrosis.

From the foregoing data, the following conclusions regarding the course of the disease seemed warranted. The tumor in the neck, below the jaw, had been devitalized and rendered quiescent. The tonsillar mass showed living tumor tissue, especially along the lower border, and the usual development of the venules offered a channel through which the disease might have become disseminated. Many of the nodules in the lung probably existed for years and had undergone spontaneous fibrosis. Many others were more recent and were somewhat active. The presence of most of the tumor masses in the wall of the chest rather than in the lung accounted for the absence of pulmonary symptoms. It is possible that the pulmonary metastases occurred several years before examination, but it may be that they began more recently, being transported direct from the vascular areas of tumor tissue in the neck. The main cause of the rapid decline was probably due to the swift course and destructive nature of the lesion in the spinal column. It was difficult to account for the extreme congestion and extensive necrosis of tissue in the spinal vertebrae.

*CASE 3—History*—A white woman, aged 50, presented herself at the Lexington Clinic, Lexington, Ky., in March, 1928, at which time she said that she had had a nasal discharge for the past two and a half years. There had been three severe nasal hemorrhages, the blood from one of which measured about 2 liters

*Examination*—Examination at the clinic revealed a widening of the bridge of the nose with marked dilatation of the alae nasi. The tumor completely obstructed the right nostril and the septum was pushed so far to the left that the left nares was also obstructed. The tumor was fungoid and bled easily.

Her general condition was poor, and her hemoglobin was only 35 per cent. X-ray pictures of the lungs revealed several areas that were interpreted as old healed tuberculosis.

*Treatment*—At operation, the tumor was found to be confined within the septal mucous membrane, which was degenerated but intact except at the right mucocutaneous junction from which the tumor mass protruded. The mass showed practically no invasion. The entire septum was removed by means of actual cautery, and four days later radium (1,000 milligram hours) was inserted.

*Course*—The patient was sent home two weeks after operation. Three months later she returned for examination, and no evidence of disease could be found in the nose. She complained of pain in the abdomen and had a palpable epigastric tumor. It was felt that the tumor might be a metastatic carcinoma, but on account of the diagnosis of basal cell carcinoma, adenoid cystic type which had been correctly returned by one of the country's most eminent pathologists, it seemed that the mass might be something other than a metastatic carcinoma, and exploratory operation was performed. A neoplasm measuring about 8 cm across was found in the superior surface of the left lobe of the liver. A biopsy was taken and the abdomen closed without further examination.

The patient was sent home and has been observed several times since. A report on May 11, 1929, from Dr. E. C. Yates of the Lexington Clinic stated that X-ray pictures of the skull were negative. Roentgen examination of the chest showed several metastatic areas, and in the right upper end of the humerus was an area of destruction due to metastases. The spine, pelvis, hips and both femurs were negative for metastases. The patient had a large tumor mass in the abdomen and had a considerable amount of pain intermittently. The patient's general condition, however, looked good. She showed a secondary anemia, urinalysis gave negative results. The local area in the nose showed no gross evidence of recurrence, but there were two small nodules in the external canthus of the right eye and one larger nodule near the left lower alar cartilage. On Oct. 31, 1929, Dr. Yates wrote: The patient had metastases to the right humerus, the remainder of the bony skeleton was intact. She also had metastases throughout her entire abdomen and her chest.

*Autopsy*—The body was that of an extremely emaciated white woman about 53 years of age. The abdomen was markedly distended, and the superficial blood vessels were prominent on the right side. A small, firm, nodular tumor was present just below the inner canthus of the right eye. Numerous, small, brown, slightly raised areas were in the skin over the side of the chest and abdomen. The peritoneal cavity contained about 8 liters of clear, amber-colored fluid. There was about 30 cc of blood-tinged fluid in the right pleural cavity. The left lung was studded with firm, grayish nodules that varied from 1 to 40 mm in diameter. The posterior portion of the upper lobe was replaced by a large mass of this firm tissue. The right lung was essentially the same as the left, but the right pleural cavity contained no fluid. The ribs were the seat of extensive metastases, being more marked on the right where the sixth and seventh ribs exhibited pathologic fractures posteriorly. Grossly, the vertebrae were negative and the head of the right femur was involved. The heart was normal. The mediastinal lymph nodes were slightly enlarged. The liver was tremendous, and was occupied by a large tumor mass and a few smaller ones. Sections through the

neoplastic tissue revealed many minute cavities and a few large spaces filled with clear fluid. The gallbladder was not unusual. The stomach was distended with gas and was closely adherent to the under surface of the liver. The inferior surface of the diaphragm was spotted with numerous, grayish-white plaques, and this condition existed throughout the peritoneum. The spleen was surrounded by firm adhesions but was not enlarged. A few small gray tumors were in the capsule and substance of this organ. The kidneys were normal, except for dilatation of the pelvis. The ureters were distended. The suprarenals showed no gross lesions. The omentum, mesentery, ovaries and fallopian tubes were masses of tumor tissue. The uterus was normal. The meninges and brain were normal. In the right side of the nose (posterior, superior and lateral portion) there was a pedunculated, irritable tumor 3 cm. in diameter.

*Histology*—Sections from the tumor in the nose revealed a basal cell carcinoma enclosing numerous small and large cysts which contained a pale staining mucoid material. The histologic structure of the tumors in the lungs, liver, peritoneum, omentum, ovaries, fallopian tubes and the ribs was identical to that of the nasal neoplasm.

*Diagnosis*—The anatomic diagnosis was primary adenoid cystic basal cell carcinoma of the nose with extensive generalized metastases.

#### SUMMARY

In the first case the tumor apparently originated in the skin of the cheek near the right nasolabial fold. It ran a slow course for years, remaining localized but finally destroyed the right ala nasi. Recurrences were persistent despite the efforts of roentgenologists and surgeons. Without any increase in the activity of the local tumor there was widespread metastases to the bones and viscera. This dramatic change was confused with multiple myeloma, for it was thought that the basal cell nature of the tumor of the skin precluded its metastasis.

Possibly the primary site of the neoplasm in the second case was in the submaxillary salivary gland, but it was thought to be separate from it. The lesion was early suspected of being an adenocarcinoma and was thoroughly operated on several times. The progress of the malady was slow but steady. Irradiation was enlisted as a last resort, and the local effect seemed beneficial, but the dissemination was wide and distant.

The mucous membrane of the nasal septum gave rise to the carcinoma in the third case. The patient did not present herself for treatment until she had had severe hemorrhages and almost complete nasal obstruction. Soon after that she had a palpable tumor in the epigastrium which proved to be metastasis, and the x-ray films revealed areas of increased density in the pulmonary fields. This patient is still living and has shown favorable effects from the treatment (surgical intervention, locally, irradiation there and to the metastases), but undoubtedly she is doomed. This case differs from the other two in sex, slightly younger age and lack of treatment until the disease was advanced.

In each of the three cases the tumor originated in supposedly different tissues, but they presented a somewhat similar histologic structure.



It is realized that the tumors may conceivably have begun in misplaced bits of tissue thus following out the Cohnheim theory, but this assumption does not seem warranted

### CONCLUSIONS

1 Adenoid cystic carcinoma is probably a distinct disease and should not be confused with adenoid cystic epithelioma as described by Brooke and Fordyce and should be regarded as different from adenocarcinoma

2 There are two general groups, both being based on whether the tumors arises from a *cutaneous* or a *noncutaneous* site. This grouping is justified by the low mortality in the former as compared to the high death rate in the latter

3 The histologic structure in the *cutaneous* and the *noncutaneous* groups is similar, and in each it closely resembles that of adenoid cystic epithelioma of Brooke and Fordyce. The cystic form of rodent ulcer is likewise confusing, and histologically may be identical with the cutaneous type of adenoid cystic basal cell carcinoma. In the *noncutaneous* tumors one must rule out adenocarcinomas and so-called mixed tumors of the salivary glands. The history and physical observations are important aids in making the differential diagnosis in each type

4 Adenoid cystic basal cell carcinoma is a radiosensitive tumor and should be treated primarily with irradiation and only secondarily with surgical procedures. One should not temporize, the therapy should be applied early and vigorously

5 Although there are well authenticated but rare cases in the literature in which ordinary basal cell carcinomas have extended to the regional lymph nodes, I have failed to find instances in which there were any proved distant or generalized metastases. That such widespread dissemination may occur is believed to be reported here for the first time. It is this feature that I particularly wish to emphasize

NOTE—Since the compilation of the data in this article, there have been several cases in which the invasion of bone by "adenoid cystic basal cell carcinoma" has occurred. This ability of this type of tumor to metastasize to bones is upheld in a case report recorded by Martin<sup>52</sup>

Most of the material came from the service of Dr. Douglas Quick. Dr. E. C. Yates, Lexington Clinic, Lexington, Ky., supplied data on one of the most important cases. Dr. Alfred Plaut of the Woman's Hospital, New York, stained some of the material for mucin. The photographs were supplied by Mr. William Dunn.

<sup>52</sup> Martin Haves E. Adenoid Cystic Epithelioma of Scalp, with Dissemination to Bones, Bull. Memorial Hospital 3 46, 1929

# TOPOGRAPHIC RELATIONSHIP BETWEEN THE NERVE PLEXUSES AND LYMPH NODES OF THE ABDOMEN \*

PROF F KISS

SZIGID, HUNGARY

The standard anatomic texts, such as those of Gray,<sup>1</sup> Bardeleben and Haeckel,<sup>2</sup> Poirier,<sup>3</sup> and Testut,<sup>4</sup> as well as the monographs of Muller,<sup>5</sup> Bartels,<sup>6</sup> Hovelacque<sup>7</sup> and others, give exact descriptions of the topography of the abdominal nerve plexuses and the abdominal lymph nodes. Up to the present, however, there has been no description of the topographic relations between the two systems. Clinical experience teaches that metastases and inflammatory processes in the abdominal lymph nodes cause various symptoms, such as pain and functional disturbances in various organs. Further, it has been seen that after operative removal of such nodes severe postoperative complications, such as paralysis and trophic disturbances, often occur. The purpose of this paper is to give a topographic-anatomic explanation for these phenomena. My studies concerning this question are all made on human material, and my illustrations in the text were also derived from the same source. In general, I have chosen for my observations cadavers (those of children and adults) in which the abdominal lymph nodes were somewhat enlarged. In preparing my specimens I used most of the modern methods,<sup>8</sup> such as dissection under water, digestion with acidol-pepsin, etc. Fresh or partially preserved material may with great advantage be kept in running water from fourteen to sixteen days during the process of dissection. By this means the connective tissue becomes edematous and remains soft, while the lymph nodes and nerve fibers retain their original consistency.

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\* Submitted for publication, Feb 27, 1930

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2 Bardeleben and Haeckel Atlas der topographischen Anatomie, Jena, Gustav Fischer, 1908

3 Poirier, P Traite d'anatomie humaine Paris, Masson & Cie, 1901

4 Testut Traite d'anatomie, Paris, Gaston Doin, 1911-1912

5 Muller, L R Das vegetative Nervensystem, Berlin, Julius Springer, 1920

6 Bartels Das Lymphgefass-system, in Bardeleben Handbuch der Anatomie, 1909

7 Hovelacque, A Anatomie des nerfs craniens et rachidiens et du system grand sympathique, Paris, 1927

8 As described in a monograph by Worobiew Methodik der Untersuchungen von Nervelementen des makro- und makro-mikroskopischen Gebietes, Berlin, Oscar Rothacker, 1927, pt 1

In the following description, I shall discuss the topographic relationship of the separated lymph node groups to the nerve plexuses. In the nomenclature of the nerve plexuses, I shall use the classification that I have published in collaboration with Ballou.<sup>9</sup>

The cardiac or paracardial lymph nodes lie in the immediate vicinity of the vagus nerves (Jamieson and Dobson<sup>10</sup>). The left group of

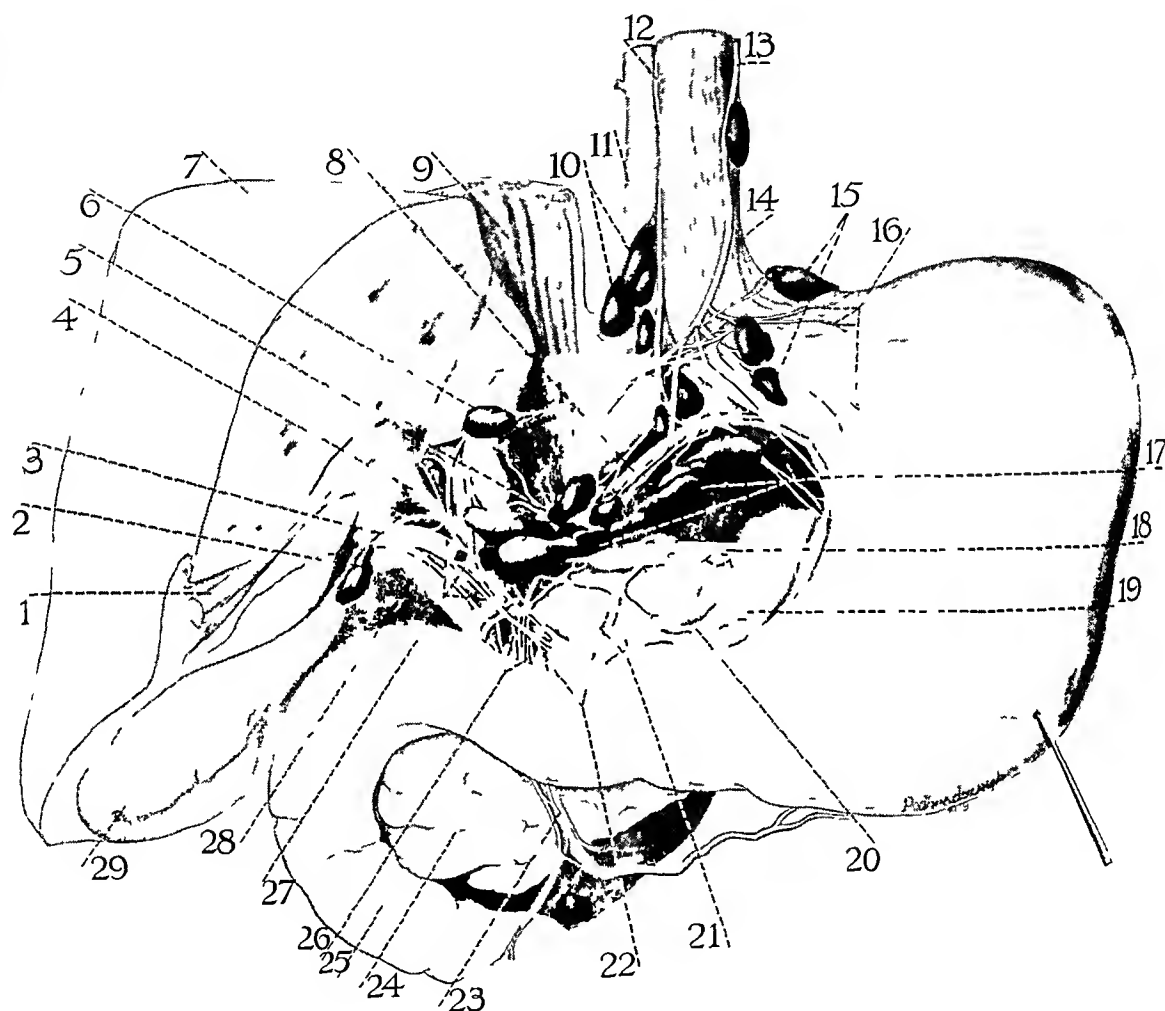


Fig 1—This figure and figures 2, 3 and 4 show the topographic relationship between the nerve plexuses and the lymph nodes of the abdomen. Here 1 indicates round ligament, 2, cystic node, 3, cystic artery, 4, hepatic artery, 5, right celiac ganglion, 6, hepatic node, 7, liver, 8, left gastric artery, 9, lumbar part of the diaphragm, 10, paracardial nodes, 11, aorta, 12, right vagus, 13, left vagus, 14, esophagus, 15, paracardial nodes, 16, cardiac branches of the vagus, 17, superior gastric nodes, 18, splenic artery and plexus, 19, pancreas, 20, splenic vein, 21, pancreatic plexus, 22, pyloric plexus, 23, gastroduodenal artery with nerves, 24, head of pancreas, 25, duodenum, 26, pancreatic plexus, 27, hepatic plexus, 28, common duct, 29, gallbladder.

<sup>9</sup> Kiss, F., and Ballou, H. C. The Celiac Plexus and Its Branches, *Arch Surg* 19 399 (Sept) 1929.

<sup>10</sup> Jamieson and Dobson in Poirier (footnote 3).

these nodes lies directly on the gastric branches of the left vagus which run along the anterior surface and both curvatures of the stomach (fig 1). Hence even the trunks of the vagi can be influenced by these nodes.

The upper gastric nodes (*lymphoglandulae gastricae superiores*) form a chain around the left gastric artery. This artery is accompanied in its course by two large branches of the vagi, one from each vagus, in addition to other small gastric branches that take part in the formation of the celiac plexus. These are the parasympathetic (vagus) roots of the celiac plexus which supplies most of the abdominal organs, such as the liver, pancreas, kidneys, suprarenals and intestine. Whether these fibers have specific cells in the celiac ganglions or merely traverse these ganglions and have their ganglion cells only in the respective organs is still an undecided question. For my observations it is important only to know that these branches are exposed to compression or irritation from inflamed (enlarged) lymph nodes. In the operative removal of the lymph nodes, injury of these important nerves is inevitable.

One group of these nodes, the right group, lies in the hepatoduodenal ligament in front of the portal structures immediately over the fine branches of the hepatic plexus. These nodes are called the hepatic lymph nodes (fig 1). They lie in the loose connective tissue of the hepatoduodenal ligament in close relationship, on the one hand, to the portal structures such as the hepatic artery, the portal vein and the common duct, and, on the other hand, to the fine nerve branches of the hepatic plexus. As Ballou and I have shown in the aforementioned publication, the branches of the hepatic plexus are exposed to manifold injuries in operations on the biliary passages. As figure 1 clearly shows, this plexus can also be greatly influenced by pathologic changes in the hepatic lymph nodes. Radical removal of the nodes can result in destruction of the greater part of the plexus. Since the lesser curvature of the stomach in the living lies much nearer to the hilus of the liver than is shown in figure 1, the branches of the pyloric plexus, the gastroduodenal plexus and the pancreatic plexus (fig 1) lie in the immediate vicinity of the hepatic nodes. The cystic node (fig 1) lies on the cystic duct, where it comes in contact with the cystic artery and the cystic branches of the hepatic plexus. If the duodenum and the head of the pancreas are grasped and these structures are pulled to the left (figs 2 and 3), important topographic relationships are seen between nerves, lymph nodes and ganglions. The posterior pancreatic nodes are seen lying on the head of the pancreas with the nerves to the head of the pancreas (figs 2 and 3). Three nodes in the vicinity of the duodenojejunal flexure lie in close connection with the origin of the large superior mesenteric plexus (figs 2 and 3). On the posterior abdominal

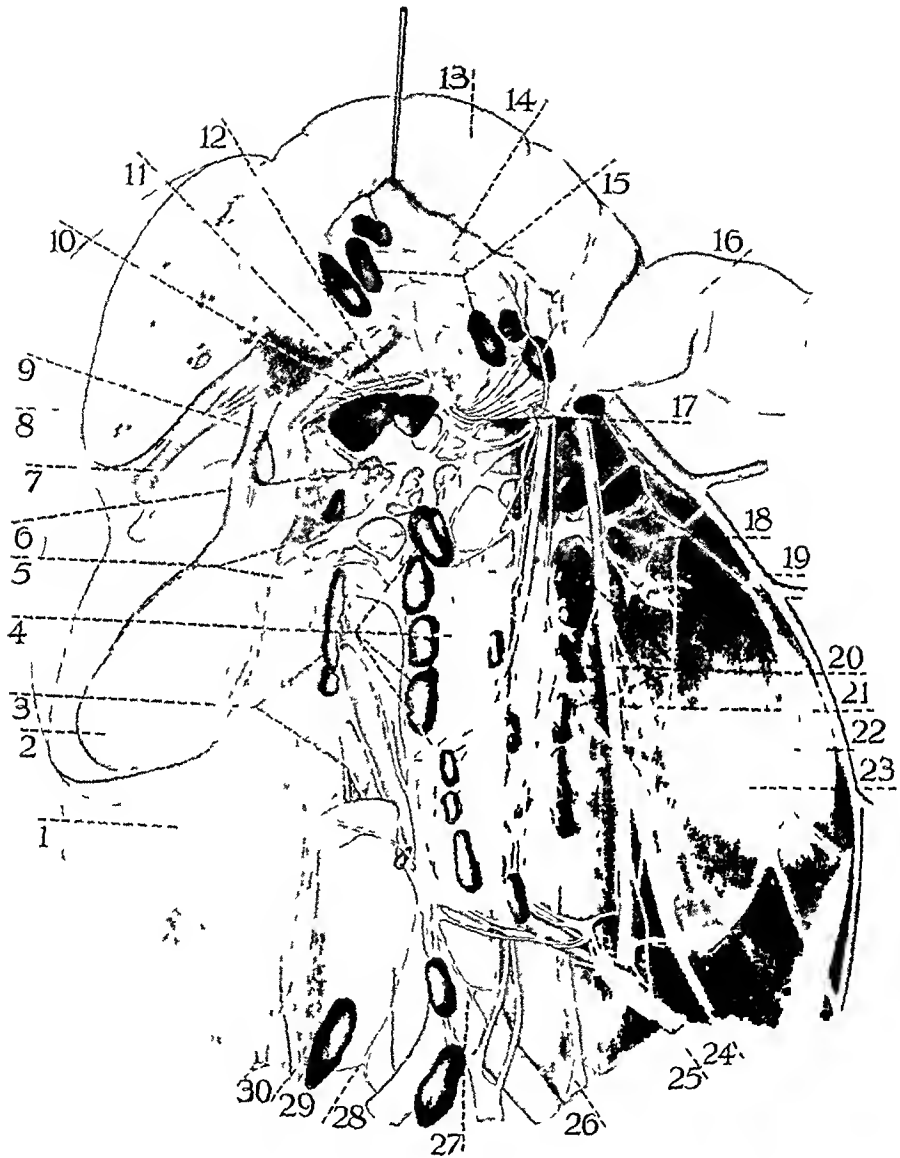


Fig 2—In this figure, 1 indicates the kidney, 2, gallbladder, 3, right sympathetic cord with retroperitoneal lymph nodes, 4, aortic plexus with aortic lymph nodes, 5, renal plexus, 6, right celiac ganglion, 7, round ligament, 8, liver, 9, cystic artery and lymph node, 10, celiac lymph nodes, 11, common duct, 12, portal vein with hepatic plexus, 13, duodenum (posterior surface), 14, pancreas, 15, posterior pancreatic lymph nodes, 16, jejunum, 17, superior mesenteric plexus, 18, left renal plexus, 19, left colic vein, 20, left aortic lymph nodes, 21, internal spermatic vessels with nerves, 22, nerve to the descending colon, 23, left kidney, 24, sigmoid vein, 25, inferior mesenteric artery and plexus, 26, left sympathetic cord, 27, aorta with aortic plexus, 28, inferior vena cava, 29, ureter, 30, right colic veins.

wall to the right of the aorta, the right celiac ganglion—a flat, soft structure—lies in the retroperitoneal connective tissue. Immediately on its anterior surface are two or three large lymph nodes (the celiac lymph nodes, figs 2 and 3). The ganglions as well as the lymph nodes in the living are covered by the head of the pancreas and the deep pancreatic nodes. It can clearly be seen from my specimens that the celiac ganglion can easily be influenced by various pathologic changes in the aforementioned nodes. Since the celiac ganglion is to be con-

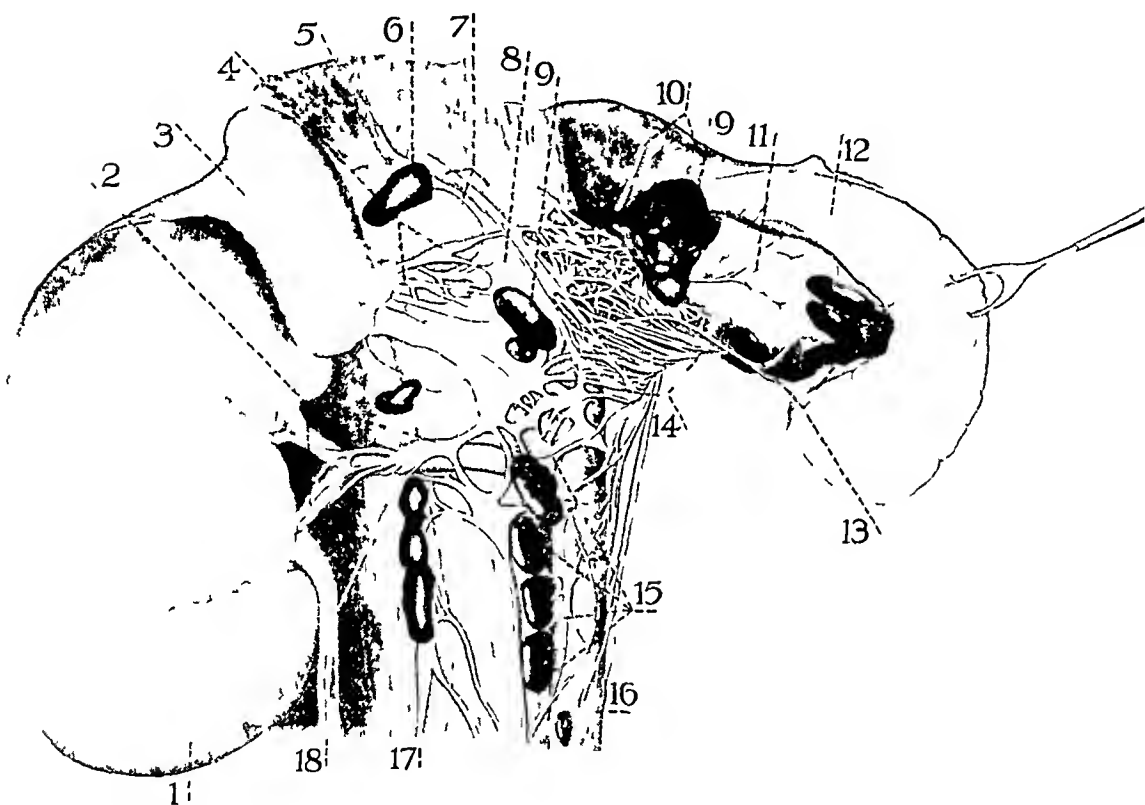


Fig 3—In this figure, 1 indicates the right kidney, 2, renal artery with plexus, 3, suprarenal body, 4, suprarenal plexus, 5, phrenic ganglion, 6, suprarenal lymph node, 7, diaphragmatic plexus, 8, celiac ganglion, 9, celiac lymph nodes, 10, hepatic plexus, 11, head of pancreas, 12, duodenum (posterior surface), 13, posterior pancreatic nodes, 14, superior mesenteric plexus, 15, aortic plexus with aortic nodes, 16, aorta, 17, sympathetic cord with lymph nodes, 18, ureter

sidered as a topographic and also partly as a physiologic center of the abdominal plexuses, it is clear that irritative stimuli of this ganglion can be referred to all abdominal organs. Figure 4 shows that the branches of the superior mesenteric plexus in the mesentery lie in close relationship to many other lymph nodes. From a topographic standpoint, however, the aforementioned pancreatic nodes as well as the celiac nodes seem to be far more important, because by influencing

the celiac ganglion and the main roots of the entire superior mesenteric plexus, they can influence the greater part of the intestines

Figures 2 and 3 show the huge aortic plexus with the numerous aortic lymph nodes. All of these structures lie in the retroperitoneal connective tissue on either side of the aorta. Smaller and larger nerves as well as the ganglions lie in close relationship to the lymph nodes

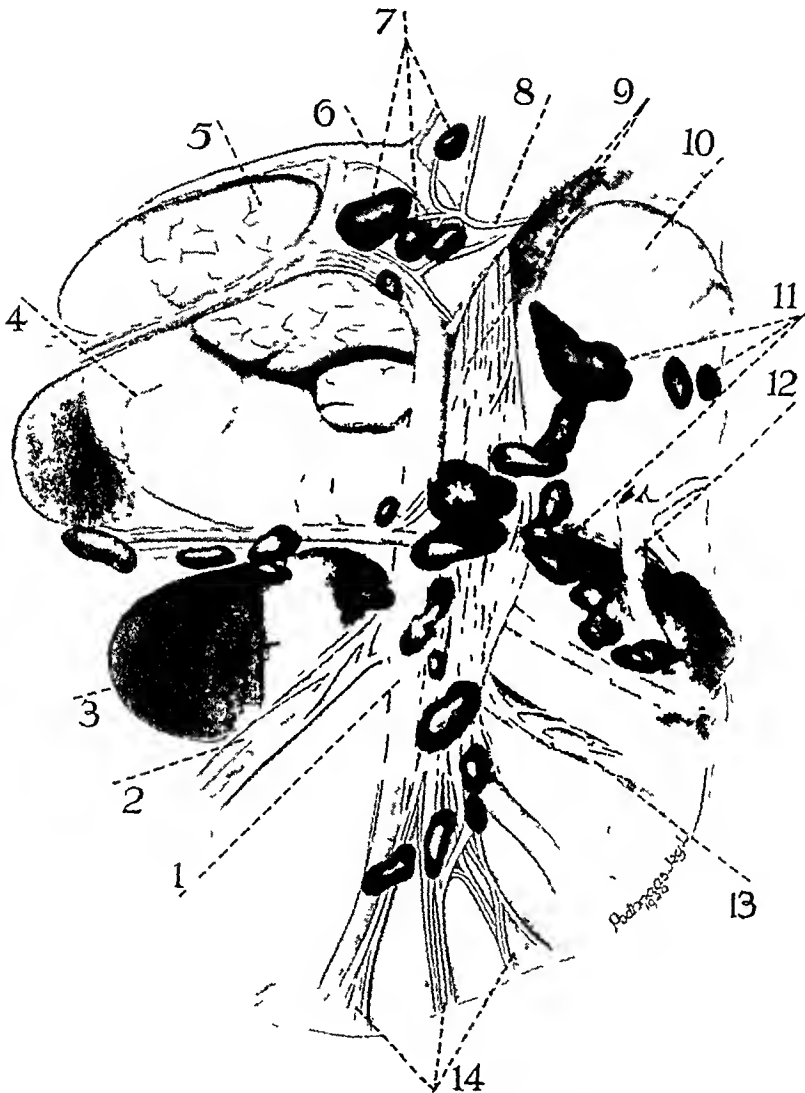


Fig 4—In this figure 1 indicates the superior mesenteric vein, 2, branch of superior mesenteric artery with nerve, 3, inferior vena cava, 4, duodenum, 5, pancreas, 6, middle colic vein, 7, mesenteric lymph nodes, 8, nerve to the transverse colon, 9, superior mesenteric plexus, 10, duodenojejunal flexure, 11, middle mesenteric lymph nodes, 12, left colic vein, 13, branch of superior mesenteric artery with nerves, 14, branches of the superior mesenteric artery and plexus (to the small intestines)

Since the dissection of the complicated nerves and lymph nodes requires a most painstaking technic it can be readily understood that the ordinary operative removal of these nodes is accompanied in every case by

appreciable injury of the nerves and ganglions. A topographic study of these structures explains the various preoperative and postoperative complications of the lymph nodes, such as referred pains, functional and trophic organic disturbances, etc. For a clear understanding of this question one must not forget that all of these nerve plexuses contain fibers from the sympathetic, parasympathetic (vagus) and spinal nerves (sensory) and probably also special trophic fibers. These separate fibers are influenced separately or simultaneously by pathologic changes in the lymph nodes.

The renal nerve plexus (figs 2 and 3) also is closely related to several lymph nodes (renal nodes).

Figure 2 shows the origin of the inferior mesenteric plexus with the one lymph node among the nerve fibers. Since the number of the lymph nodes varies in different persons, a greater number of nodes may be found in a special case than any of the foregoing illustrations have shown.

Figure 3 further shows the suprarenal and the diaphragmatic plexuses which also are closely related to the nodes shown in figures 1 and 2.

The superior mesenteric plexus in the radix mesenterii surrounds the trunk and the branches of the superior mesenteric artery (fig 4). As figure 4 shows, innumerable mesenteric nodes lie directly on the nerve fibers, and some are even between the fibers.

#### SUMMARY

- 1 The abdominal lymph nodes lie in close topographic connection with the ganglions and nerve plexuses.

- 2 Pathologic changes in the lymph nodes, such as hyperemia and enlargement, may cause various nervous symptoms, such as irritation, paresis, etc.

- 3 The ordinary operative removal of diseased lymph nodes may result in various injuries to the nerves and ganglions. This explains various postoperative complications after such operative procedures.



# THE ETIOLOGY OF NEOPLASMS OF THE BREAST

WITH NOTES ON THEIR RELATION TO OTHER TUMORS OF  
THE REPRODUCTIVE SYSTEM \*

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NEW YORK

Special Aspects of the Physiology and Histology of the Normal Breast

The Ovary's Influence on the Physiology of the Breast

The Ovary's Effect on the Histology of the Breast

Special Characteristics and Relationship of Pathologic Growth Processes in the Breast

Theories of Eugen Albrecht on the Organoid Nature of Tumors

The Architecture of Tumors in Relation to Etiology

The Relation of Breast Neoplasms to Those of Allied Organs

The Supposed Causes of Origin of These Tumors of Allied Organs

The Cause of Certain Semineoplastic Growth Processes in the Breast

Experimental Evidence on the Nature of the Cause of Tumors of the Breast

Previous Views on the Origin of Tumors of the Breast

Clinical Study

Classification

Age Incidence

Degree of Breast Development

Previous Breast Disease

Abnormalities of Ovarian Function

Associated Pelvic Disease

Associated Thyroid Disease

Physical Examination of the Breast

Notes on General Physical Constitution

Heredity

Histologic Form of Cancer of the Breast in Relation to Etiology

Resume

My purpose in this paper is to examine the evidence in support of the theory that a functional disturbance of the physiologic relationship between the ovary and the breast is an important factor in the genesis of many forms of tumor of the breast

Since the literature on mammary neoplasms already contains the reports of many scattered observations and a few definite studies that favor such a contention, an important part of the present undertaking must be the coordination of some of the recorded material into what is hoped may be a logical conception

The histologic aspect of neoplasms of the breast has received the attention of the pathologists of several generations so that it appears

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\* Submitted for publication, Oct 30, 1929

\* Aided by a grant from the Mrs John L. Given Fund

\* From the Memorial Hospital

unlikely that much further progress can be made at present by means of morphologic studies. For this reason, I will be content with previously described and for the most part accepted pathologic structures and will concern myself only with the attempt to correlate these structures with the physiologic conditions under which they occur.

The clinical approach to the etiologic problem has also received much attention, but such studies made with a constant regard for the precepts of breast physiology have been few and imperfect. Yet the correlation of special disturbance of function with particular deviations in form may well be at the root of the tumor problem, and until more exact methods have been devised, the abnormalities of breast physiology are best discovered by the clinical history of its past performance and the determination of its physical condition and that of its associated organs.

The view that specific physiologic disturbances are concerned in the production of tumors suggests at once that many errors may have been made by students of mammary neoplasms on account of a prejudice in favor of the irritative agents that have been satisfactorily demonstrated as predisposing to cancer in other organs and a scant regard for the physiologic differences inherent in the breast cells. The result of comparing the tumors of the breast with those of other organs can be made to lead to quite different conclusions. The tissue which evolves cancer most definitely in response to external irritation is squamous epithelium, whose normal function of the protection of underlying soft parts is evoked by this type of stimulus. The epithelioma can therefore be regarded as the result of an excessive reaction to the specific stimulus to which the squamous epithelial cell is physiologically best adapted to respond. If such a conception is correct, one must look for a different type of stimulus for the tumors that arise from the glandular tissues of the breast.

This study of the evidence leading to the belief that an endocrine disturbance is an important factor in the causation of tumors of the breast is presented in the following form:

- 1 A consideration of the stimulus which normally produces proliferation in the breast shows that it is the ovarian secretion to which the breast cell is specifically responsive throughout life.

- 2 A consideration of the changing histologic structure of the breast shows that many of the pictures incidental to a normal response of the parenchyma of the breast to the ovarian secretion differ only slightly from that of certain neoplastic processes.

- 3 Attention is drawn to the fact, illustrated particularly by the work of Eugen Albrecht, that tumors resemble organs both as regard their structure and their behavior, and very likely their origin.

- 4 An analogy is offered between the tumors of the breast and those of the other parenchymatous organs of the reproductive system. For many of these

tumors an ovarian dysfunction has been suggested as causative, for a few it is nearly proved and has displaced an older inflammatory theory

5 The evidence is given to show that certain hypertrophies and hyperplasias of the breast that lie on the borderline between physiologic and neoplastic growth are probably dependent on ovarian dysfunction

6 A few of the features of the biology of tumors of the breast in animals and their behavior under experimental conditions, are cited mainly in support of an internal causative factor

7 The chief previous theories of origin of fibro-adenoma, "chronic mastitis" and carcinoma are discussed

8 A clinical study of 271 cases of mammary tumors is offered as a preliminary survey of the field of ovarian disturbance in relation to the genesis of tumors of the breast

## SPECIAL ASPECTS OF THE PHYSIOLOGY AND HISTOLOGY OF THE NORMAL BREAST

### THE OVARY'S INFLUENCE ON THE PHYSIOLOGY OF THE BREAST

In the study of the causes of abnormal cell growth in the breast, it is essential to consider first the stimuli that produce normal cell growth, or, to place the emphasis more correctly, the stimuli to which the cells of the breast are physiologically adapted to respond

The modern theories in regard to the physiology of the breast were formulated by Josef Halban in a study published in 1905. In this work, based chiefly on an extraordinary array of clinical facts and observations, he came to the conclusion that the ovary was the cause of breast growth except during pregnancy, when the placenta performed this function, but that secretion was a totally different process and was due to the loss of the growth stimulus and was actually the beginning of involution.

Halban's conception of the life history of the breast's activity is that of a long wave extending from birth through puberty and maturity to the menopause with secondary waves, superimposed on it, the latter being the cyclical periods of premenstrual activity and the irregularly placed waves of pregnancy and lactation. The physiology of these phases of breast development shows clearly the conditions favorable to the proliferation of breast cells.

(A) *Breast Activity in the Prenatal and Neonatal Periods*—Swelling and secretion of the breasts is observable in the majority of newly born children of both sexes (Lindig, Hoeland). For many years it has been believed that the cause of this infantile breast secretion must be nearly identical with that of the simultaneous maternal mammary activity (Knoepfelmacher). This view was amplified by Halban's studies of the breasts of premature stillborn infants which showed that there was some proliferation intra-utero as early as the eighth or ninth lunar month. This fetal breast activity Halban ascribed to the effects

of "the pregnancy substance" reaching the fetus through the placenta. In spite of some dissent (Lindig), there seems little reason to doubt that this postnatal secretion affords the earliest example of a proliferative response of the breast to a hormonal stimulation. This view has received important support from a very recent study of Philipp, demonstrating a folliculin-like substance in the blood and urine of newly born children.

(B) *Breast Development at Puberty*—That the development of the breast at puberty is dependent on the presence of an active ovary has long been indicated from the failure of the breasts to develop in women with infantile or absent ovaries and in animals castrated before breast growth has occurred.

Positive evidence of the dependence of the breast on the ovary for its development has been given by two types of experimental procedure—organ transplantation and the use of organ extracts. The earlier work with transplantation was performed by Knauei, in 1900, and Halban, in 1903, both of whom found that the reimplantation of ovaries in castrated animals resulted in a new development of the mammary gland. Later, Steinach and Athias were able to produce breast growth even in male guinea-pigs by this method. The production of hyperplasia of mammary glands in castrated and later in immature animals in response to various extracts of the ovary and placenta has been accomplished by many workers, among whom may be mentioned Frank and Unger in 1911, Fellner in 1913, Herrmann in 1915, and more recently Steinach and Laqueur with their co-workers.

The determination of the special structure within the ovary from which arises the substance that produces the breast growth at puberty is of theoretical interest only in the present clinical study (Steinach, Lipschutz, Allen and Doisy). On the other hand, it is essential to note the apparent physiologic state of the sexual function under which breast growth occurs. The studies of Stratz and of Weissenberg have shown that there are slight indications of breast growth in the tenth year, and that by the fifteenth, when practically all girls have well developed breasts, still one third have not menstruated. It should therefore be clear that the fully developed follicle-corpus luteum apparatus is not essential either to the initiation of breast growth or to its considerable development and it is in fact an intermediary stage of ovarian activity, before menstruation has become established, that is most favorable to the proliferation of breast tissue.

(C) *The Menstrual Activity of the Breast*—The participation of the breast to some extent in the changes of the menstrual cycle is indicated clinically from the consideration of the many women who complain of premenstrual sensations in their breasts such as pain

tenderness and at times moderate enlargement. There are even instances such as the case reported by Schweitzer, of a definite cyclical period of milk secretion at the time of the menstrual flow.

Studies in the field of animal experimentation indicate also that there is a definite influence exerted on the breast by the corpus luteum. Bouin and Ancel were able to demonstrate this on the rabbit by observing hypertrophy of the breast in association with artificial corpora lutea produced by mating a virgin female with a sterilized male. Other authors, including Frank and Unger, O'Donoghue, Hammond and Marshall, and Loeb and Hesselberg, made similar observations on mammary gland growth in relation to the formation of corpora lutea. It has, of course, been repeatedly demonstrated that in several animals proliferation of breast tissue follows the injection of corpus luteum extracts.

To correlate these observations with the normal condition in the human breast it is only necessary to point out that several studies (Frank and Goldberger, Hirsch) have demonstrated a rise in the ovarian hormone content of the blood from the time of ovulation at the middle of the intermenstrual period to the onset of menstruation at which time a rapid disappearance takes place. This period of relatively high hormone concentration in the circulation corresponds with the time of corpus luteum growth and the clinical signs of premenstrual breast activity. Finally, histologic changes confirm the existence of a monthly cycle in the breast.

(D) *The Breast Development During Pregnancy*—It has usually been considered necessary to divide the activity of the breast during pregnancy into two phases, that of proliferation and secretion or of preparation and function, and most authors have recognized that an essential difference must exist between the causes of these fundamentally separate processes.

(1) *Proliferation Phase*. Halban thought that the placenta was the cause of proliferation during pregnancy, and, except for its neglect of the part played by the corpus luteum in the early months of pregnancy, his theory remains valid today.

(2) *Secretion Phase*. Lactation is apparently the result of the cessation of a preceding stimulus to proliferation for it is known to occur after parturition after abortion and after delivery of an hydatidiform mole and microscopic evidence of slight secretion is found after the onset of menstruation (Ernst, Moszkowicz). That the placental activity is antagonistic to the breast's function was proved by Frankl when he prevented lactation in mice by means of placental transplants. Since secretion occurs only when the stimulus to proliferation ceases, some authors have regarded lactation as a kind of physiologic cellular degeneration or beginning involution (Hildebrandt).

Not only at the onset of lactation but throughout its course are there evidences of antagonism between breast function and placental or ovarian activity. This antagonism is illustrated most dramatically by the observed disappearance of the milk supply under the influence of a new pregnancy but it has also been shown (St Engel) that in women whose breasts have been secreting insufficiently, menstruation (ovulation) returns in the first few months post partum. Cohn has observed an increase in milk secretion in a puerperal woman on whom bilateral oophorectomy was performed for osteomalacia. Keller referred to similar results following castration in cattle. Inversely, Parkes and Belleby, working on mice, believed that they could obtain a diminution in the milk supply by the injection of estrius-producing hormone.

The effect of the ovary on the clinical course of lactation must, therefore, be great, and this must be borne in mind in interpreting various points in the lactation histories in cases of cancer. Postpartum engorgement of the breast may be the result of excessive hypertrophy and as such have no inflammatory significance. A short nursing period due to defective milk supply is dependent on a developmental anomaly or on early return of ovulation and is not proof that there has been chronic irritation from stasis of secretion. Even puerperal mastitis or "caked breast" may be in part due to some internal stimulation, for in such a case observed at the Memorial Hospital Clinic rapid improvement followed with the onset of the impending menstrual period.

(E) *Breast Activity at the Menopause*—The cessation of ovarian activity is accompanied in the breast by a gradual atrophy of the parenchyma and its replacement by fat and fibrous tissue. Yet certain reservations must be noted.

The disappearance of ovulation as manifested by the menstrual periods is frequently very irregular. Such irregularities when due to special abnormalities of ovulation have been related to endometrial hyperplasia and are perhaps equally related to hyperplasias of the breast.

After the cessation of menstruation, it is probable that slight ovarian activity continues for a time from the cells of the atretic follicles or related structures. There is thus again for a short time a condition of partial ovarian activity as there was at puberty when breast growth is so marked.

Finally, in rare cases there may be a late return of menstruation or at least a pathologic condition of the ovary having the ability to affect the endometrium (Schiffmann, Meyer).

*Summary of Notes on Physiology*—1 The hormone of the ovary or placenta is the agent to which the parenchyma of the breast is normally adapted to respond with proliferation.

2 The effect of the ovary is felt by the breast from before puberty until after the menopause, but it is especially during the periods of partial activity when there is no menstrual cycle (prepuberty, pregnancy) that the greatest hypertrophy occurs

3 Breast secretion is apparently a passive phase and evidence only of a preceding stimulation that has partly or completely disappeared

#### THE OVARY'S EFFECT ON THE HISTOLOGY OF THE BREAST

A study of the histology of the normal breast, particularly in its various phases of activity reveals many structural forms that are found also in certain neoplastic diseases of the breast and points to a semphysiologic basis for the latter

(A) *Histology of the Breasts in the New-Born*—The histologic similarity of this early physiologic hyperplasia to that of the abnormal hyperplasias of later life has been particularly emphasized by Cheate, and indeed many of the structures present in "chronic mastitis" have their counterparts in the infantile breast. Dietrich's recent studies show that in newly born children the breasts contain hypertrophied glands with a two-layered epithelium surrounded by a loose connective tissue partially differentiated from the supporting stroma. Evidences of secretion in the form of fat droplets are present in the lumina of the ducts and in the epithelial cells (Hoeland). Round cell infiltration is mentioned by many writers (Berka), but since it parallels the secretory function it is usually regarded as a resorptive mechanism. Finally, it is interesting to note that Dietrich observed two cases of microscopic cyst formation which he regarded as the result of an incomplete involution following this infantile lactation.

(B) *The Histology of the Breast in Relation to Puberty*—The histologic changes at puberty consist in a marked increase in parenchyma with the differentiation about the epithelial elements of a specialized loose connective tissue, variously known as periacinar or mantle tissue (Berka). An island of glands with its stroma is known sometimes as a lobule or by many German authors as a "gland field." Aside from this primary growth of epithelial and connective tissue, there are again at times signs of secretion in the breast, and Cheate noted a temporary return of the lymphocytes.

The rapidity of this growth at puberty and the degree of development attained shows marked individual variations, and Dieckmann has demonstrated that the microscopic structure of the breasts of women of the same age shows great differences in the complexity of the duct and gland systems. Such differences are important for they probably account in part for the clinically observable variations in the response of the mammary glands of different women to the stimuli of the menstrual cycle and pregnancy.

(C) *The Histologic Effect of the Menstrual Cycle on the Breast*—The first histologic studies on the relation of the human breast to the sex cycle were published by Rosenberg in 1922. This work was based on the examinations of breast tissue obtained at autopsy and correlated with the phase of the sexual cycle as determined by the history of the time of the previous menstruation, by the apparent age of the most

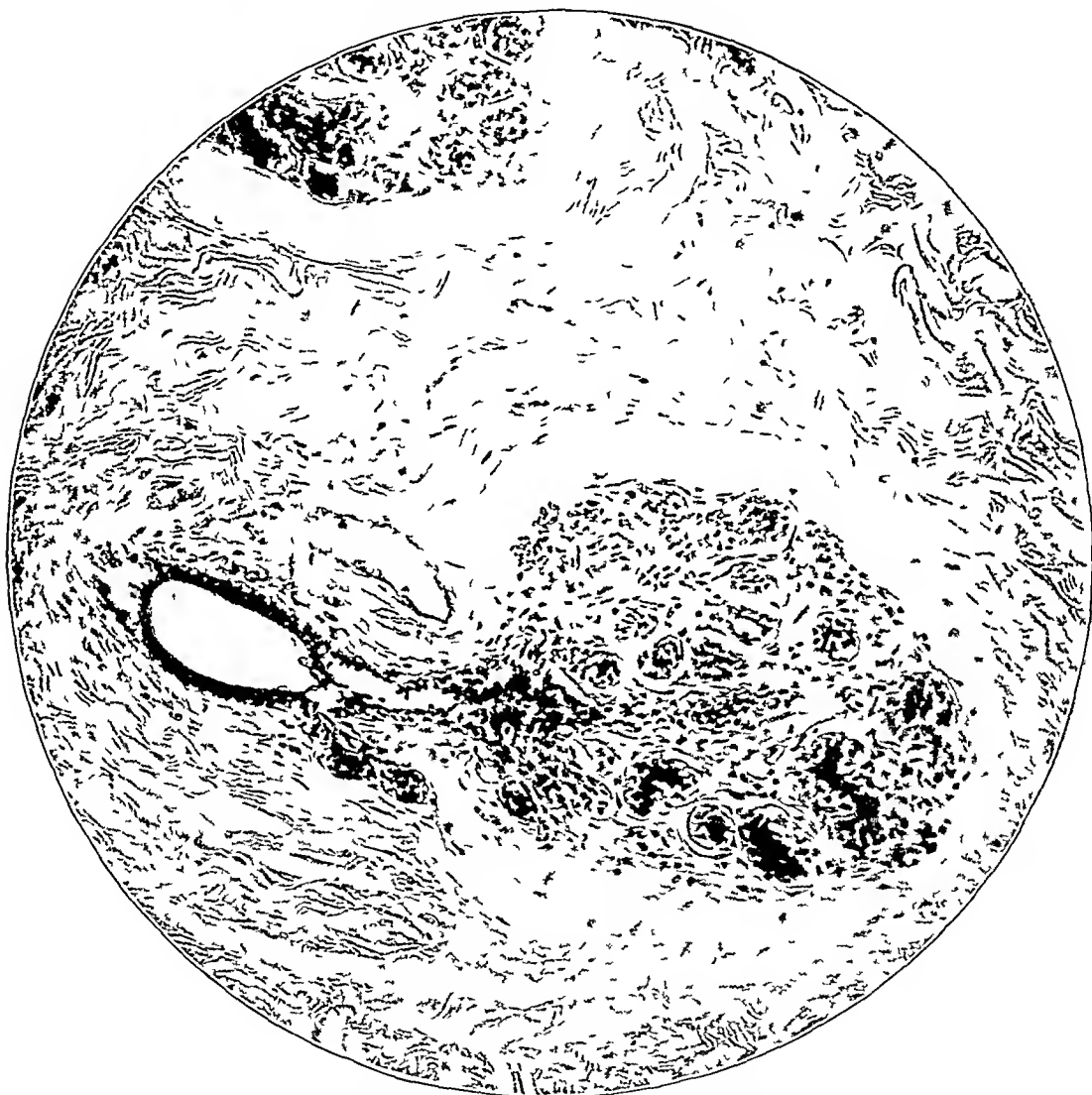


Fig 1—Premenstrual hypertrophy of the breast, typical gland field, magnification  $\times 125$  (After Rosenberg Frankfurt Ztschr f Path, Munich [J F Bergmann] 27 466 1922)

recent corpus luteum and by the examination of the endometrium. His conclusions indicated an actual sprouting of the milk ducts during the premenstruum and an almost complete regression in the interval so that at that time only milk ducts existed in the breast (figs 1 and 2). Rosenberg definitely ascribed the premenstrual proliferation to the corpus luteum.



Rosenburg's work received a certain degree of confirmation from the studies of several writers (Polano, Ernst, Beiberich and Jaffe), but there has also been strong opposition. Dieckmann was able to find little evidence of epithelial change and noted only a premenstrual loosening up of the mantle tissue and a lobular edema, resulting in a more striking demarcation of the gland fields. Moszkowicz agreed

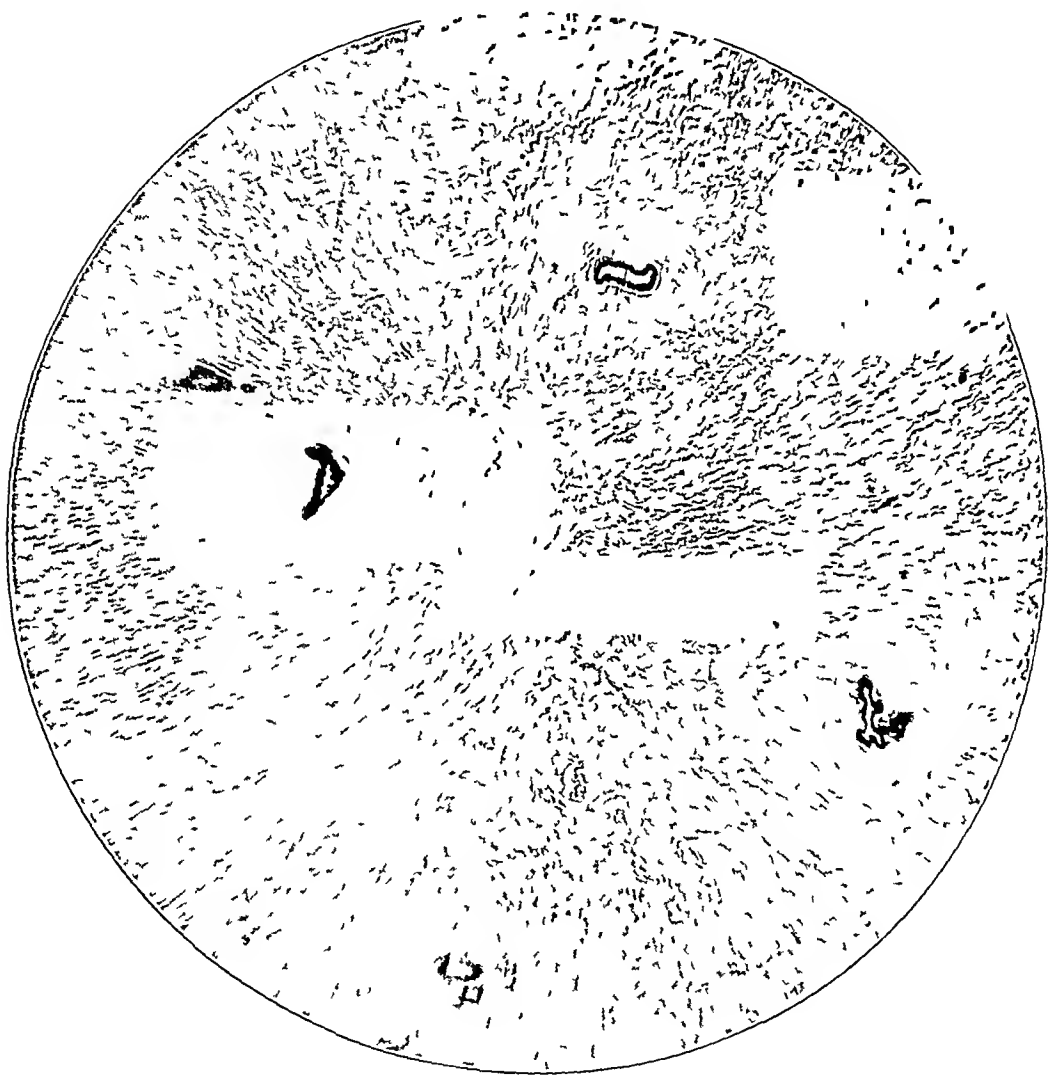


Fig 2—Breast in the interval stage, magnification  $\times 18$  (After Rosenberg Frankfurt Ztschr f Path, Munich [J F Bergmann) 27 466, 1922)

with Dieckmann in finding no direct evidence of epithelial growth but stated as his opinion that some such growth might nevertheless occur and that the actual completion of breast development after puberty might take place during this monthly period of stimulation from the corpus luteum.

The existence of a functional as well as a proliferative phase of activity was emphasized by the studies of Ernst and Moszkowicz. The

former observed that during the menstruum and post menstruum there occurred an infiltration of lymphocytes and plasma cells into the periductal and periacinar tissue that corresponded to the infiltration of cells into the tissues of puerperal women in whom there was stagnation of the breast secretion. He concluded, therefore, that these cells had a resorptive function. Moszkowicz confirmed this recurrent cyclical invasion of round cells and stressed also the occurrence of a definite although transitory fat secretion from the epithelial cells, a process which reached its height during the time of the uterine flow.

The important question of whether an actual proliferation of breast epithelium occurs each month must be considered undecided although the weight of recorded evidence seems now to be slightly against it. There remains the possibility that such extreme degrees of activity occur only in the special type of women who suffer from severe premenstrual breast symptoms. There is some histologic evidence to support such a view for Sebening, in studying the tissues lying adjacent to twelve localized tumors removed for the complaint of "painful nodule," reported that although complete regression in the interval was never observed as Rosenburg had claimed, there was, on the other hand, invariably evidence of epithelial sprouting during the premenstruum.

(D) *The Histologic Changes in the Breast Incidental to the Stimuli of Pregnancy and Lactation*—The development of the breast during pregnancy is described by Berka as consisting of two stages. In the first half of pregnancy there is a rapid proliferation of the epithelium in solid budlike processes that later differentiate into acini. Simultaneously, there is an increase in the mantle tissue which at this period is very cellular and packed with lymphocytes and plasma cells. In the latter half of pregnancy the epithelium takes the form of definite dilated alveoli. The connective tissue is pushed aside and the cellular infiltration largely disappears (Berka). After parturition there is a great increase in the gross size of the gland, but it is doubtful if new acini are actually formed in the puerperium (Berka).

At the end of the nursing period, three histologic processes become apparent: (1) the collapse of the acini with shrinkage and then degeneration of the epithelium, (2) a new proliferation of the periductal tissue (McFarland), (3) a new lymphoid invasion (Berka). The latter process was especially studied by Gruber, who observed the round cells in all breasts in which there was stasis, and construed their function, as Ernst later did for the lymphoid cells incidental to the menstrual phase in the breast as having to do with the removal of cell debris and secretion.

An interference in this normal process of involution was considered by McFauland to have much to do with the production of the condition known as chronic cystic mastitis, since he considered the cystic structures in this disease to be what he termed "residual lactation acini." It is not quite clear to me whether or not McFauland chose to bind himself to the theory that all multiple cystic conditions in the breast were due to a previous pregnancy. Such a contention is untenable. It has already been pointed out that Dietrich found cystic dilatation in the breasts of infants. Askanazy referred to several instances of cystic breasts in children, in girls at puberty and even in males. The many causes of hyperplasia and even of breast secretion make it seem more plausible to suggest that such cystic dilatations may be the "residual acini" of a previous hyperplasia of some type, whether pathologic or physiologic, but not necessarily of a fully developed lactation.

(E) *The Histologic State of the Breast in the Menopause*—It appears probable that in only a few breasts is the normal course of gradual parenchymatous atrophy followed continuously after the menopause. Instead, several writers who have studied supposedly normal breasts have reported a considerable percentage with signs of irregular epithelial proliferation. Those signs of growth commonly met with, according to Berka, are the multiplication of the cell layers, a subdivision of lumina of glands by anastomosing cords of epithelial cells and the final filling up of the lumina of the ducts with solid masses. Tietze reported such changes in 25 per cent of grossly normal breasts and Goens found atypical growth in twenty of sixty breasts at autopsy on a series of women over 40 years of age. Such changes as those noted by these authors in the breasts of the older women are, of course, identical with some of the histologic changes in cases of so-called chronic mastitis. The vital question to be asked is whether, after the menopause, one is to discard the type of stimulus that throughout life has caused proliferation of breast tissue and for these older breasts find an entirely new agent.

*Summary of Notes on Histology*—1 Epithelial proliferation occurs under physiologic conditions in response to an ovarian or placental stimulation.

2 Connective tissue changes are coordinated with the glandular and are either dependent on an epithelial control or result from similar intrinsic causes.

3 Evidences of secretory activity appear invariably after the cessation of a proliferative stimulus.

4 Round cell infiltration, as a rule, accompanies secretion and is to be regarded as a physiologic resorptive mechanism.

5 Cystic dilatation may be the result of incomplete involution from several types of hyperplasia

## SPECIAL CHARACTERISTICS AND RELATIONSHIPS OF PATHOLOGIC GROWTH PROCESSES IN THE BREAST

### THEORIES OF EUGEN ALBRECHT ON THE ORGANOID NATURE OF TUMORS

Before passing to the discussion of the causes of pathologic growth processes, it is necessary in transition to emphasize the close relation between development of normal tissue and neoplastic growth. The theories of the nature of tumors propounded by one writer twenty or more years ago give such an excellent basis for this point of view that they deserve special attention.

Eugen Albrecht, in his papers on "*Die Grundprobleme der Geschwulstlehre*," stressed organization as the essential characteristic of tumors. It is this quality which demonstrates the relation of neoplasms to organs and distinguishes them from simple cellular multiplication. Benign and malignant tumors differ only in the degree in which they manifest this quality, for some organization, as for example, vascularization, is seen in the least differentiated new growths. Furthermore, the chief characteristic of malignancy—namely, the tendency to infiltrative growth—is, as Ribbert had also pointed out, merely the faithful reproduction of the invasion by embryonic cells of the undifferentiated matrix in the course of formation of the earliest anlagen of organs.

Such an "organoid" conception of neoplasms, Albrecht believed, makes the investigation of tumors a branch of the study of the mechanism of development, and therefore, in searching for the origin of new growths, one may consult those laws which bring about the formation of normal organs in the course of normal development. As a result of this point of view, Albrecht recommended the following procedure: first, the analysis of the architecture of the particular tumor; second, the study of the relation of the growth to the organ from which its originating cells must have sprung; finally, by the comparison of its function and structure with those of the normal organ to draw from the nature of the abnormality conclusions on the causes which may have led to it.

This was an ambitious program and can be followed only in part. It has been shown in the physiologic section that all normal development of the breast was dependent on variations in the ovarian function, and the attempt will be made to indicate that new growths of the breast, as "organoid" structures, are largely dependent on a similar stimulus.

## THE ARCHITECTURE OF TUMORS IN RELATION TO ETIOLOGY

The conventional system of classification of tumors has been evolved chiefly with the view of defining types of clinical behavior. Such a system is not entirely satisfactory for an etiologic study, for it tends to isolate special tumor forms and thus conceals the points of relationship between different neoplasms.

The following may be mentioned as among the more important of the factors which cause variations in tumor architecture and which are of quite unequal importance so far as an etiologic classification is concerned: (1) localization or diffusion of the process, (2) functional state of the tumor cells, and (3) degree of differentiation of the tumor cells. It must not, of course, be imagined that these factors are not interrelated.

The factor of degree of localization is recognized in the separation of benign neoplastic processes into adenomas and hyperplasias. It is a justifiable division etiologically in so far that one must recognize a difference in the localization of the predisposition or of the action of the exciting agent. Yet there is a fundamental similarity, for each form represents a new growth of a tissue characteristic of the organ from which it arises and each exhibits similar potentialities for continued growth or evolution. Furthermore, there are many transitional forms and the localized and diffuse processes may occur in association, as in the breast where microscopic adenomatous nodules may be found developing in areas of chronic mastitis (Bloodgood).

Evidences of functional activity and associated signs of regression or degeneration account for many differences in tumor form that bear little or no relation to the ultimate cause of their origin. That the ratio of connective to glandular tissue in the fibro-epithelial tumors of the breast may be dependent on an entirely physiologic factor is suggested by several cases cited by Deaver and McFarland which led them to the conclusion that a "pure adenoma" was merely a fibro-adenoma in a state of lactation hypertrophy. In Cheatle's case of "pure adenoma" there is no suggestion of a preceding pregnancy, but in the case of a growth so highly organic in structure as the fibro-adenoma there may be other physiologic stimuli capable of secondarily influencing its structure.

To a somewhat different category belongs the development of cysts, the presence of which often dominates the anatomic picture of a tumor but which appear frequently to be due to a disturbance in drainage or absorption coupled with a continuation of the function of secretion and thus to have little actually to do with the neoplastic process itself.

The customary division of tumors into benign and malignant has been developed from a study of morphology in relation to clinical

results, and hence is based essentially on the criterion of prognosis. Such a division has not necessarily any significance from an etiologic standpoint. The recent histologic studies on the varying grades of malignancy in cancer have demonstrated that the adenoma malignum, of the endometrium, for example, is far more similar structurally to an active hyperplasia than it is to the diffusely growing carcinomas of grade III with which it is somewhat arbitrarily associated since both are called "cancer." Yet on account of the existence of this gradual transition in form, from the clearly benign to the definitely malignant, it appears unlikely that, at the point of cellular maturity where clinical malignancy begins, a new biologic process has its inception or an entirely new provocative factor becomes operative.

From the considerations of the foregoing paragraphs it appears that all of the fibro-epithelial neoplasms of the breast may be looked on as representatives of the same basic process, varying quantitatively from each other in respect to several special factors. The study of the origin of special tumor forms becomes, therefore, not a search for the separate causes of several entities, but an examination of the factors causing a tendency of tissues to approach one or the other morphologic extreme. With this reservation, it is useful, however, to recognize three type forms, the localized benign tumors, diffuse hyperplasias and carcinomas.

#### THE RELATION OF BREAST NEOPLASMS TO THOSE OF ALLIED ORGANS

The suggestion has been made that in the study of the origin of tumors of the breast special consideration must be given to the ovarian secretion, because it is to this agent that the breast is normally responsive. The breast, however, is only one of a group of organs the hypertrophies of which are under the control of the sexual function. A survey of the theories of origin of the tumors arising in these other organs related to reproduction affords a valuable check on the study of the breast, for it appears probable that an exciting agent of at least the same general type must be a factor in the production of neoplasms throughout the group.

The reasons for believing that, in respect to the tumor problem, one may regard the breast, the endometrium, the ovary, the thyroid and the prostate as forming an ill defined group are as follows:

(A) There is a similarity of the physiologic causes of hypertrophy in these organs.

(1) *Uterus*—It is in the endometrium that the greatest similarity to the parenchyma of the breast is noted, for this tissue shows activity at the time of birth (Halban, Schroder), develops at puberty, responds to the corpus luteum of menstruation and of pregnancy, and normally atrophies at the menopause.

(2) *Ovary*—As regards the ovary, the analogy immediately weakens for it is only with certain accessory and perhaps abnormal ovarian structures that comparison with breast tissue may be made, since the specific ovarian cells must be considered the primary seat of the stimuli affecting the system of secondary tissues now under consideration. The structure of the ovary that has been most definitely proved to be largely controlled in its physiologic activity by the sexual cycle is the heterotopic endometrial tissue, the so-called endometrial implant (Sampson) which is known to follow closely the endometrium in many of its reactions (Robinson).

(3) *Thyroid*—The close relation of the thyroid to the sexual function is shown by the clinical and histologic evidence of hypertrophy of the organ occurring simultaneously with similar activity in the breast and uterus. Thus there is enlargement of the thyroid at birth (Gloor), more marked, of course, in goitrous districts (von Gierke). There is increase in its size before the first menstrual period (Gundobin), which led Heidenreich to refer to a "struma antemenstrualis". There is almost certainly slight enlargement of the thyroid in many women before menstruation (Weidenmann), and in animals histologic changes have been reported in relation to the estrus cycle (Engelhorn). For many years, thyroid hypertrophy during pregnancy has been well recognized (Freund, Lange), and there is now a considerable literature on the subject in this country (Ward, Thompson, Yoakam). Certain histologic changes in pregnancy are also reported (Bell, Engelhorn). The effect of the menopause on the thyroid has been variously estimated; some authors claim an increase in activity (Schonlein, Heidenreich), others considering that the response to the menopause is variable in different women (Curschmann, Wiesel), a form of behavior having its counterpart in the irregular reaction of different breasts to the disappearance of the ovarian secretion.

It may, of course, be objected that the cause of hyperplasia of the thyroid is related to lack of iodine, but such a deficiency may be due either to a low intake or to an excessive requirement by the body, and it is on account of a relative deficiency of the latter type that hypertrophy occurs during certain periods of sexual activity (Marine).

(4) *The Prostate*—The opportunities for cyclical fluctuations in the prostate are fewer than for the other organs, but there is development at puberty and normally atrophy in old age (Simmonds, Tenenbaum).

(B) There are certain mutual similarities of structure to be noted in the organs under discussion.

The parenchyma of the breast, the endometrium and the endometrial islands in the ovary each consists of branched tubular or alveolar glands lying within a special type of loose cellular stroma, and each has the ability strikingly and rapidly to change its morphology under the influence of changes in the ovary. The prostatic glands are not dissimilar, and though having no specific periacinar stroma its glands are also found buried in a fibromuscular supporting tissue. The histology of the thyroid alone is essentially different, but at least in comparative anatomy there is evidence of a relation to the genital organs for Gaskell has suggested that the thyroid is derived from the uterus of the palaeostracans, prehistoric forms, from which he traces the origin of the vertebrates.

(C) In each organ a similar series of tumors are recognized which possess a mutual similarity in constitution and structure.

(1) *Localized Benign Tumors*—There are, of course, certain obvious differences in the structure of the circumscribed tumors as they appear in the different organs but these differences are readily laid to the variations in the structure of the tissue from which they arise and in each case the type of deviation from the normal is the same. Two of the principal differences may be explained as follows

(a) The character of the stroma and its quantitative relation to the amount of epithelium in the tumors is approximately the same as in the normal organs. Thus in the thyroid there are adenomas, in the uterus adenomyomas and in the breast as a rule fibro-adenomas.

(b) The type of cyst which so often dominates the gross appearance of these tumors is perhaps dependent on the mechanism of disposal of the secretory products. Thus, in the endometrium with a simple duct system, the cysts are small, in the breast they may be larger, and in the ovary without ducts, the cysts may become immense.

(2) *Diffuse Hyperplasias*—The diffuse hyperplasias exhibit a more confusing structure often combining with the essential proliferative process evidences of involution and even of chronic inflammation. Here, too, the fundamental similarity of the process as it appears in different organs becomes more evident if due allowance is made for certain structural differences in the original tissues that must be carried over to the neoplasms and for secondary variations due to differences in function and functional arrangement.

Within the group of related hyperplasias must be included the so-called "chronic cystic mastitis", endometrial hyperplasia, certain multicystic processes in the ovary and possibly endometriosis, colloid goiters with secondary hyperplasia and benign prostatic hypertrophy. An essential similarity between individual members of this group has been noted by many writers.

Bloodgood (1906) considered the possibility of "semile parenchymatous hypertrophy" of breast and of the prostate as of possibly the same origin as toxic thyroiditis.

Theile (1908) found a relation between chronic cystic mastitis, prostatic hypertrophy, small cystic degeneration of the ovary and goiter.

Cuttat (1912) considered prostatic hypertrophy a true fibro-epithelial degeneration having its analogy in certain fibro-epithelial tumors of breast and thyroid. Niemeyer (1921) also pointed out the resemblance between prostatic hypertrophy and the so-called mastitis chronica cystica.

Oertel (1926) has published a histologic study illustrating the similarity of the involutional and proliferative changes occurring in the breast at the menopause and in the aging prostate. He also pointed out that such changes were formerly regarded as inflammatory and hence the old names "chronic mastitis," "prostatitis" and "chronic endometritis."

Pulvermacher (1918), in the same breath, uses the terms "mastitis climacterica" and "strumitis climacterica."

Aschoff summed up this point of view by writing that "mastopathia cystica" (chronic mastitis) is a dysplastic process similar to the adenomiosis of the uterus, the adenomiosis of the prostate, the adenofibrosis of the thyroid, all of which processes particularly affect the concerned organs in the beginning of the involutional period.

In diffuse hyperplasias as they affect the organs in question there are four processes of which only one is of cardinal importance.



(a) *The Formation of Multiple Cysts* There has been considerable written to favor the view that the small cysts are to be regarded as incompletely involuted remnants and often witnesses to an antecedent phase of activity. McFarland's theory that cystic disease of the breast is the result of incomplete involution of lactation acini has been touched on. Marine has shown that the colloid acinus in the thyroid is one that has been hyperplastic and has not been able to return to its original form. The multicystic ovary is regarded as a subnormal organ, the term often used being "cystic degeneration." Cystic changes in the endometrium are usually associated with hyperplasia and occur just before the menopause. The ectasia of the alveoli which Billroth regarded as the chief epithelial change in prostatic hypertrophy tends to occur in the male involutional period.

(b) *Round Cell Infiltrations* The presence of round cells have in the past been taken as strong evidences of an inflammatory origin of the various processes in question, but there is probably much better reason to regard them as mere secondary phenomena, as part of the semiphysiologic mechanism of resorption of secretion in breast and prostate, as a result of necrosis of excessively hyperplastic tissue as in the endometrium (Schroder) or possibly simply as an accompaniment of rapid tissue proliferation.

(c) *Increase in Connective Tissue* The increase in connective tissue is probably in part due to the age replacement of parenchymatous by fibrous tissue, but in other instances it must be regarded as an integral part of the hyperplasia and developing in a certain organic relation with the epithelium as is the case in the circumscribed tumors.

(d) *Epithelial Hyperplasia* Epithelial hyperplasia remains the essential feature of these conditions, is responsible for their other morphologic features, for their clinical importance and is the process for which the cause must be examined.

(3) *Carcinoma*—Certain pathologic features of the carcinomas of these organs point to a further biologic similarity within the group.

(a) There is a close anatomic relation to the benign forms.

(1) The histologic structure of the benign forms passes almost imperceptibly into the malignant.

(2) Areas of malignant growth are frequently found arising from or associated with benign tumors or hyperplasias. Such associations of cancer with benign forms have been reported as follows: with chronic mastitis, Tietze, Oertel, Goens, MacCarty, etc., with fibro-adenoma, Speese, with endometrial hyperplasia, Meyer, Schroder, Fluhmann and Stephenson, with adenomyoma uteri, Cullen, with papillary cystadenoma of the ovary, Taylor, adenoma of the thyroid, Graham, Crane, prostatic hypertrophy, Tietze, Oertel, Neller and Neuburger.

(b) Many of the carcinomas of these five organs are intraductal or intracystic papillary tumors in their early stages, and what is especially characteristic is that their origin is frequently multicentric. For cancer of the breast, a multicentric origin has been affirmed by Askanazy, Tietze, Pribram and Lukowsky. For the bilateral papillary cystadenocarcinomas of the ovary, multiple points of development appear almost obvious. For the endometrium, Lahm wrote that he regarded a more or less diffuse origin as characteristic due to the fact that this tissue acts as a unit even in response to the stimuli producing malignant changes. Multiple cancer foci have been described in the thyroid by Langhans and noted in the prostate by Ewing.

(c) A final small but interesting similarity is seen in the special tendency to metastasize in the lungs and bones manifested by cancers of the breast, thyroid and prostate.

THE SUPPOSED CAUSES OF ORIGIN OF THESE TUMORS OF  
ALLIED ORGANS

An attempt has been made to show that the tumors of the breast are closely related to a large group of neoplasms that develop in the glandular organs related to the reproductive function. It will now be pointed out that the history of the views on the origin of many of these neoplasms has shown a gradual shift away from inflammatory conceptions toward theories based on internal causes, and in some instances specifically on abnormalities of the ovarian function.

(A) *Uterus*—(1) Endometrial Hyperplasia. The endometrium presents, of course, the most perfect physiologic parallel with the parenchyma of the breast. As is still the case in the breast, the hyperplastic disease of the endometrium was disguised for many years as an inflammation under the title of "chronic endometritis" (Ruge, Scanzoni, Olshausen), and except for an isolated work of Biennicke in 1882, remained as such until Schröder and later Mayer related pathologic hyperplasia to anomalies in ovulation. As with chronic mastitis, hyperplasia of the endometrium may occur at any time during the sexually mature period of life but is most common shortly before the menopause (Schröder, Babes, Novak and Martzloff) and is rare after the climax. A peculiar type of endometrial hyperplasia is that developing late in life in association with ovarian tumors (Isbruch, Neumann, Meyer). In one such case Schröder observed carcinoma in the endometrium.

(2) Adenomyosis Interna. The diffuse penetration of the inner muscular layers by endometrial glands was also at first regarded as an inflammation on account of the teaching of Robert Meyer who used the term "adenomyositis." Frankl later showed there was no real evidence of inflammation and used the noncommittal term "adenomyosis." More recently, Meyer has changed his view and now believes that adenomyosis interna is the result of a hyperregeneration of the basal layer of the mucosa due to the too frequent demands made on the endometrium by menstruation in the latter part of sex life. Adler and Lahn have expressed somewhat similar views.

(3) Localized Uterine Tumors. The adenomyoma, the tumor most comparable with the fibro-adenoma of the breast, has been studied chiefly with regard to the ultimate origin of its cells and with little consideration for the causes of its development as a tumor. As the type of localized uterine tumor, it appears better to discuss briefly the fibromyoma, particularly since the frequent finding of glandular islands in the midst of apparently purely muscular tumors (MacCarty and Blackmann) makes it appear that a close relation must exist between these new growths and the adenomyomas (Freund, Orloff).

That the ovary, particularly an abnormally functioning ovary, is partly responsible for the growth of uterine fibroids was suggested by Seitz, in 1911. Part of the evidence that has at various times been cited in support of such a theory is as follows: the presence of a high percentage of ovaries with pathologic changes in association with myomas (Seitz), the high incidence of myomas just before the menopause, the special predisposition of women with dysmenorrhea or sterility to develop fibroids (Mayer), the special occurrence of this form of tumor in malformed or hypoplastic genitalia (Freund), the alleged hereditary factor (Aschner, lit.), the supposed existence of a special constitutional type (Freund, Aschner), the diminution in the size of myomas after the menopause or castration.

(4) *Carcinoma of the Endometrium*—In spite of the similarity of structure between endometrial hyperplasia and adenoma malignum, there has been considerable hesitancy in claiming an endocrine dysfunction as a factor in the production of corpus carcinoma. One author (Lahm) at least wrote that he found the origin of corpus carcinoma in the enormous capacity of the uterine mucosa for transformation on the one hand, and on the conditioning of this transformation by the ovarian hormone on the other. This view receives a little support from the frequent history of sterility and the common association of fibroids in cases of corpus carcinoma.

(B) *The Ovary*—In his original paper on extra-uterine endometrial growth, Lauche regarded the serosal endothelium as the parent tissue and ascribed its metaplasia to the ovarian function, chiefly because the disease occurred exclusively in the years of sexual maturity. This age incidence can also be accounted for by Sampson's theory of transtubal implantation, but it appears that even with this conception an ovarian secretion is in a sense necessary, for it is known that an endometiosis tends to regress after castration.

If the heterotopic endometrium is actually the result of a metaplasia of the serous epithelium (Meyer, Robinson) and not an implant, it becomes the simplest member of a series of neoplasms derived from the germinal epithelium and falls into a similar genetic group with various cystic tumors of the ovary. That many serous papillary cystadenomas and cystadenocarcinomas are associated with signs of ovarian dysfunction has been pointed out in a previous paper.

(C) *Thyroid*—The endemic occurrence of goiter is somewhat reconciled with the facts of enlargement of the thyroid due to glandular dysfunction by Aschoff's conception that the thyroid in goiter regions is so sensitized that it responds excessively and permanently to the normal physiologic stimuli.

That hypertrophy of the thyroid and certain nodular goiters may be associated with an ovarian disturbance is indicated by the following points

- (1) The predilection of thyroid disease for women
- (2) The tendency of goiters to develop at periods of irregular ovarian stimulation, at birth, at puberty, during pregnancy and at the menopause
- (3) The association with toxic goiters of menstrual irregularities or amenorrhea under which circumstances it has been suggested by some of the older writers (Pinard, Trousseau) that it is the ovarian disturbance which is the primary
- (4) Thyroid hypertrophy may be associated with definite pelvic disease, a point especially emphasized in this country in the writings of Hertzler. Such associated genital conditions have been myomas (Thompson, Freund, etc.), tuberculous peritonitis (Goodall and Conn), excessive sexual indulgence (Goodall and Conn, Freund)

(D) *The Prostate*—The theories in regard to benign prostatic hypertrophy have followed a course similar to that of chronic mastitis. Many authors have been satisfied to debate the nature of the process, and it has accordingly been variously termed a neoplasm (Virchow, Gardner and Simpson), a compensatory hypertrophy (Simmonds), a fibro-epithelial degeneration (Cuttat). As regards the actual cause of benign prostatic hypertrophy, Ciechanowski formerly strongly advocated an inflammatory theory, maintaining that the disease resulted from a chronic gonorrheal infection which, by producing a scar tissue that constricted the ducts, terminated finally in glandular dilatation and stasis of secretions. An entirely different theory is that of Simmonds who expressed the belief that a presenile atrophy of the prostate results in a lack of prostatic secretion, which is followed by a compensatory hypertrophy of the periurethral glands, the proliferation of which into the old prostate results in the enlargement. Variations of this theory have been expressed by MacEwan, Moullin, Niemeyer and others.

There are two other aspects of the biology of the tumors under consideration which give additional evidence for an internal causative factor.

1. There is a tendency for the benign neoplasms to regress somewhat after the sex gland has been removed. In the uterus one sees this process in the successful treatment of myomas, endometrial hyperplasia and possibly very early endometrial carcinoma by irradiation, a procedure that probably has its effect by way of the ovary. Peritoneal endometriosis and the multiple peritoneal implants from papillary cystadenoma of the ovary may disappear after double oophorectomy. Diminution in the size of an hypertrophied prostate has been reported after castration and at one time was even suggested as a therapeutic measure (MacEwan, White, Moullin, Simmonds). The effects of castration on cancer of the breast are to be discussed in detail. The

effects of castration on goiters is apparently variable and seems not always to be beneficial

2 Evidences of an hereditary influence have been found for many of the benign hypertrophies and tumors of all of these organs and such a factor has been suggested for the malignant ones. For the uterus one finds many reports of the occurrence of myomas in families (Mayer, Aschner, lit.) For the thyroid, the subject of hereditary backgrounds is well discussed by Brain, Siemens, Valley-Radot and others. The latter considers the hereditary factor to be in the nature of a constitutional glandular predisposition. For the ovary dermoids alone appear to occur in families. For the prostate, Simmonds stated his belief in an hereditary predisposition to benign hypertrophy.

One gains the impression that vague as any evidence for the inheritance of tumors may be, it is rather greater for the new growths of these glandular organs associated with reproduction than for neoplasms elsewhere and, should this be the case, it would appear that the hereditary factor is linked with a special constitution of the glands connected with the reproductive apparatus.

*Summary*—1 Tumors of the breast are allied to the neoplasms of several other glandular organs connected with reproduction.

2 The normal causes of the proliferation of the tissues of these organs are similar, and a comparable series of neoplasms is produced in each.

3 On account of these similarities, it is unlikely that the neoplasms of one of the organs of the group should be produced by a totally different type of stimulus from that believed to be operative in the other organs.

4 There is a growing tendency to ascribe the cause of many of the new growths of these organs allied to the breast to the anomalies of the sexual function.

#### THE CAUSE OF CERTAIN SEMINEOPLASTIC GROWTH PROCESSES IN THE BREAST

The ovarian function can be brought a step nearer to the problem of tumor growth in the breast by a consideration of the causes of certain abnormal processes that lie on the borderline between the physiologic and the truly neoplastic.

(A) *Pubertas Praecox*—That breast growth may occur at an abnormal period of life under the influence of ovarian disease is shown by the cases of precocious breast development in association with the growth of ovarian tumors (Termeer). The relation between ovarian tumor and breast growth is apparently a direct one for the mamma-

enlargement may disappear after the pelvic tumor has been removed (Harris). It is interesting to note that the so-called precocious puberty associated with suprapneal disease is rarely productive of breast changes (Nemeth-Glynn-Krabbe).

(B) *Massive Hypertrophy*—The enormous breast growth that occurs in this disease appears frequently to be the result of abnormal ovarian function. Greig, for example, records disorders of menstruation, especially scanty menses and amenorrhea coincident with the onset of the hypertrophy. Plummer and Pamp, in reviewing the cases of the so-called adipose type, found abnormal menstruation in five of the six known cases. Blond likewise, in summarizing all the cases that had been reported with pathologic records, concluded that the cause of the hypertrophy lay in anomalies of the ovarian function.

The relation of massive hypertrophy to the true neoplasms is probably very close. Bloodgood brought forth the interesting point that 'cystic adenoma' bears the same relation to 'simple parenchymatous degeneration' (chronic mastitis) that fibro-adenoma does to diffuse vaginal hypertrophy. He mentioned the development of carcinoma in a case of hypertrophy, and similar malignant changes were reported years ago by Atken and Billroth. Atken's case report is especially interesting from the standpoint of the present paper, for his emphasis of the fact that evidences of 'intermenstruation' were present at the time of the appearance of the cancer shows that a possible relationship of tumors of the breast to pelvic disease was not unthought of in 1825.

(C) *Painful Breasts*—To this category belong those breasts which become painful and swollen in the week before menstruation. The possible relation of these symptoms to an actual premenstrual glandular proliferation has been discussed. An association of this condition to pelvic disease has been noted by Miller, who found a palpable gynecologic lesion in 50 per cent of his patients with painful breast nodules. Temesvary cited two cases of the older English authors (Percy, Copland), who many years ago had connected mastodynia with uterine and ovarian disorders. It is likewise not an uncommon observation at the Roosevelt Hospital gynecologic clinic that many patients with a subsiding pelvic inflammation pass through a stage in which they suffer from menstrual irregularities and breast symptoms. For certain of these painful breast conditions corpus luteum has been recommended (Lisser), but a few patients so treated at the Memorial Hospital have shown only a questionable improvement.

(D) *Lactation in the Nonpuerperal Breast*—Lactation in the nonpuerperal breast is related to the present subject from two angles.

1. Secretion from the nipple is often carelessly regarded as sufficient evidence to make a diagnosis of chronic mastitis, and hence the cause

of this secretion is also the cause of a certain number of cases clinically labeled with that diagnosis

2 The cause of the visible secretion from the nipple is probably the same as the secretion that is detectable on section in the ducts of many diseased breasts, and which is the stagnating medium on which in older women the "stasis" theory must depend

Milk has been found in the breasts of nonpuerperal women during certain phases of the sexual cycle and in association with many forms of pelvic disease. The following conditions may be noted: (1) in relation to the menstrual cycle (Schweitzer, Gautier, Ciamei), (2) following removal of the ovaries (Allsberg, Grunbaum), (3) in the menopause (Ebele, Litten), (4) with amenorrhea from injuries (Cohn, Vogt), (5) with ovarian disease (*a*) inflammation (Hallauer, Ebele, Ballin), (*b*) tumors (Saenger, Polano Schmincke), (6) with fibromyomas (Freund, Heischan, Ballin, Ebele)

In general, it appears that in the nonpuerperal breast, secretion occurs in the presence of a diminishing function of the ovary as it does under all physiologic conditions

(*E*) *Gynecomastia*—Deaver and McFarland reported from their careful study of gynecomastia that the disease occurs particularly in association with imperfect development of the sexual organs, pseudohermaphroditism, with atrophy or removal of the testicle. Other reports have mentioned hypernephroma (Busch), prostatectomy (Mann), tumor of the testicle (Heizenberg, Monaschkin). A case seen at Memorial Hospital developed in a young white man about fifteen months after marriage in association with a typical exophthalmic goiter. There seems little doubt, therefore, that many cases of abnormal growth processes in the male breast are also related to disorders of the sexual function

#### EXPERIMENTAL EVIDENCE ON THE NATURE OF THE CAUSE OF TUMORS OF THE BREAST

The extensive study of the etiology of the mammary tumors of some of the lower animals has yielded many important facts which cannot be disregarded in determining the course that the research in tumors of the breast in man should take

(*A*) *The Inheritance of Cancer of the Breast in Mice*—That strains of mice may be bred in which practically all of the females will develop cancer of the breast if they survive to a certain age has been repeatedly demonstrated by a multitude of experiments, although the exact mechanism of the inheritance may still be in dispute (Little, Slye)

(*B*) *Protection from Cancer by Oophorectomy*—A series of experiments initiated in 1916 by Lathrop and Loeb have shown that in a

tumor-bearing strain of mice the rate of tumor incidence may be lowered and the average age of onset raised by the prevention of breeding and by castration. Loeb, in 1919, amplified these experiments, finding that there was a more or less definite relationship between the number of estrus cycles that the mouse was allowed to pass through before oophorectomy and her chances of developing cancer. Coit, in 1927, confirmed these results and noted that tumors were entirely prevented by castration under twenty-two days and the normal rate of incidence was unaffected when operation was delayed until the animals were 6 months old. Murray, in 1928, using male mice of a stock in which the females showed a high tumor incidence but in which the males were never affected was able to produce cancer of the breast in 15 of 210 animals that had been deprived of their testes at the age of from 4 to 6 weeks and supplied with an ovary by transplantation from a sister. Loeb believed that the protective effects of gonadectomy were due to the removal of the corpus luteum which is responsible for the periodic stimulation of the breast tissue to growth.

(C) *The Development of Multiple Tumors of the Breast in Dogs*—In support of Albrecht's conception of the organoid nature of tumor growth Jaeger, in 1910, published a report on three cases of multiple mixed tumors of the mammae in dogs. In each case the tumors had appeared in immediate connection with "menstruation" and two of the animals, although recently mated, had failed to conceive. Jaeger considered these coincidences so unusual as to point to the conclusion that the origin of the tumors must be referred to a disturbed activity of the reproductive organs.

(D) *Studies in Relation to the Functional Activity of the Breast in Mice*—Starting with a strain of mice carefully inbred, with a well known low rate of tumor incidence, Baggs has increased the incidence by subjecting the breasts to various abnormalities of lactation, such as rapid repetition of pregnancies without suckling. Such results could apparently with equal justification be ascribed to the effects of the too rapid repetition of pregnancy hyperplasia or to the irritation arising from the congestion and stasis resulting from the failure to nurse.

Baggs was also able to induce the development of cancer in the breasts of a certain number of lactating mice by ligation of the nipple. This appearance of cancer following obstruction to the flow of milk is certainly in favor of a "stasis theory," but the implications from the experiment can have only a limited applicability to the problem of tumors of the human breast so few of which originate in immediate connection with lactation.

(E) *The Production of Tail Cancers in Rabbit Breasts*—Cheatele has made a point of the similarity between the reactions of the skin to



the application of tar and the series of epithelial hyperplasias which he has described as occurring in the breast. He cited this as support for his belief that these breast conditions are also the result of a local irritant. In view of this argument, it is interesting to note that the injection of various tar preparations into rabbit breasts by Yamagiwa and Murayama resulted only in the production of a certain number of cases of "cancroid and adenocancroid." The authors themselves write "We found that the secreting glandular epithelia do not respond to the irritation of tar but soon perish. For this reason we were unable to produce true glandular carcinoma."

It may be a fact of very great significance that tumors in mice with their strong hereditary influence and their characteristic of being affected in their incidence by oophorectomy are glandular cancers as in women, whereas attempts to produce cancer in breasts of rabbits by a local irritant result only in epitheliomas.<sup>1</sup>

(F) *The Effect of Castration on Carcinoma of the Breast in Women*—Near the beginning of the present century, oophorectomy for inoperable cancer of the breast attained a short vogue. The rationale of this treatment was logically arrived at by Dr. G. T. Beatson, who had observed a certain resemblance between the mammary changes in pregnancy and those of early cancer and hoped accordingly that castration might produce a fatty degeneration in the cancer cells. Beatson's first few cases in which this method of treatment was used were reported in 1896 and gave evidence of at least a temporary beneficial effect from the operation.

Following Beatson's original article, the operation was repeatedly attempted and about a hundred cases were reported in England by Hermann, Boyd, Thompson and Lett, a few cases in Germany by Cahen and a few in America by Robert Abbe. The reports of many of the writers mentioned emphasized that oophorectomy produced the best results when performed on women developing cancer before the menopause and also that the greatest diminutions in size following the treatment were to be expected in the relatively slow growing tumors producing local recurrence without metastasis. Since such behavior is that of the more differentiated histologic forms of cancer of the breast the response described is quite analogous to the regression of the semimalignant implants on the peritoneum following bilateral oophorectomy for papillary cystadenoma of the ovary.

#### PREVIOUS VIEWS ON THE ORIGIN OF TUMORS OF THE BREAST

The general classification of the epithelial neoplasms of the breast into the fibro-adenoma "chronic mastitis" and carcinoma offers three types of neoplastic processes for study. A word must be said about the previous ideas on the nature and origin of these special forms

(A) *Localized Benign Tumors*—Most authors agree that all the benign, solid encapsulated tumors of epithelial and connective tissue, in whatever proportion, belong genetically to a single group. Certain writers (Cheatele, Charlatow) appear to separate the so-called "pure adenoma" slightly. Wilms regarded all these growths as mixed tumors in the strict sense, namely, that they are derived from anlagen segregated from both germinal layers. Ribbert also classed these tumors as fibro-epithelial but not actually "mixed," for he implied only that epithelium and connective tissue were growing in mutual interdependence. Albrecht classed the fibro-adenoma as a "hemartome," a form due to a defective mixture of the constituent tissues but closely allied to the normal organ.

Another point of view was taken by Beneke who was greatly influenced by the then popular doctrines of Roux on the dominating role played by the epithelium in the determination of tissue form (see also the recent discussion by Fischel). After studying the parallelism between fetal breast development and the formation of benign tumors, Beneke concluded that the epithelium was the primary and guiding factor in both instances, and for him all fibro-epithelial tumors were essentially adenomas. Other authors prefer to place the emphasis on the connective tissue component. In a recent article on benign tumors of the breast, McFarland recommended the term suggested by Warren, namely, periductal fibroma, for the common type of localized benign tumor. Cheatele, though not permitting himself much theorizing, appears from his minute descriptions of the histologic effects of hyperplasia "intra-elastica," "extra-elastica" and "elastica" to place a high degree of importance on the connective tissue changes.

In the consideration of the localized tumors, it appears obvious that one must consider two processes: (1) the cause of the segregation of the special group of cells which give rise to the tumor and (2) the reason for the development of these germs. Whether the germs of the mammary tumors become differentiated from the rest of the tissue during fetal life or later, must remain a theoretical consideration. Since the puberty period of the breast corresponds with the fetal stage of many of the body organs, it would not be inconsistent with the theory of embryonal segregation of tumor germs to suggest that possibly the differentiation of certain growth foci takes place at that time. The cause of the further growth of fibro-adenomas is certainly in part connected with the sexual function, for such tumors make their appearance as a rule soon after puberty and are extremely unusual in childhood, after the menopause or in the male breast. More direct evidence for a special ovarian dysfunction as productive of fibro-adenomas is cited under the discussion of the endocrine origin of "chronic mastitis" since most authors have discussed the two conditions together.

(B) *Diffuse Hyperplasia*—"Chronic Mastitis"—The cause and nature of this disease have been a popular subject for scientific debate for at least thirty years. The early studies of Cooper, Brodie, Velpeau and Reclus were chiefly independent and excited little antagonism, but, in 1892, Schimmelbusch published a work calling the disease a "cystadenoma," and in the following year Koenig proposed the title "mastitis chronica cystica." Thus the lines were drawn between two distinct theories, inflammatory and neoplastic. In the next few years, both views received support and attempts at modification from many writers. For the inflammatory theory may be mentioned Roloff, Lichtenhahn, Maly and Delbet, for the neoplastic, von Saar, Bissaud, Cornil and Keibel. Certain authors such as Sasse and Curtis and Wood found evidence of both processes being active.

As it gradually became obvious that the disease could not be categorically classified, new attempts were made to define microscopically the nature of the changes. As a result, some authors have emphasized particularly the epithelial proliferation, among which have been Berka, Tietze, and more recently, Cheate. Other writers have considered as primary the connective tissue changes, this being the view supported by Greenough and Haitwell, Dietrich, Todyo, Berthels, Lever and Lukowsky. With the former, the disease became an epithelial hyperplasia closely approaching true tumor growth, with the latter a fibromatosis often connected with the general presenile changes.

The chief views on the etiology of chronic mastitis that appear still to have a claim to consideration are as follows:

(1) *Theory of Malformation*. This theory rests chiefly on the studies of Krompecher who came to the conclusion that the cysts of acidophilic cells in the breast were similar to the sweat gland cysts of the axilla, and as he regarded such cysts as the most characteristic feature of "chronic mastitis" he decided that this disease represented an atavistic malformation in the direction of sweat gland form. Krompecher's theory has received very little confirmation by other writers and has been contradicted by Askanazy, Lukowsky and others.

(2) *Theory of the Stasis of Breast Secretion*. This theory is the modern version of the older inflammatory view of origin of chronic mastitis. The theory takes two forms, dependent on the theoretical source of the stagnating substance:

(a) *Stasis of the secretions of lactating breast due to faulty nursing*. Adair and Bagg have emphasized this as a factor in the cause of cancer in their study of the nursing histories of 200 women with carcinoma and have also demonstrated the effect of stasis by the already cited experiment of the ligation of the nipple in mice. Keynes believed that the earlier incidence of chronic mastitis in single women was due to the lack of proper drainage usually afforded by a pregnancy.

(b) The stasis of the secretion of the nonlactating breast Keynes based his case on the fact that there was always some secretion in the milk ducts and on his demonstration of the complete obstruction to the outflow of this material through the presence of a plug of desquamated epithelium that under ordinary circumstances completely closes the orifices in the nipple. According to Keynes, the cause of the epithelial changes in "chronic mastitis" lies in the chemical irritation of the stagnated secretion. To prove that such material may incite proliferation, he cited A. H. Diew, who had shown that cellular growth was stimulated by the products of autolysis. Keynes believed that there was no relation between this breast disease and involutional changes, but two of his predecessors in the stasis theory, Berthels and Lukowsky, placed the primary change in the connective tissue, which by its constriction of the ducts prevented proper drainage.

The stasis theory depends much on the histologic evidence supplied by the presence of the round cell infiltrations to show that a chronic irritation exists. The semiphysiologic significance of these round cells has been previously touched on.

(3) Involution Theory. Involution cysts were mentioned by Billroth, in 1880, but the idea that the whole process was connected with involution has been slow to develop and has taken many different forms. In 1905, Warren designated the condition usually called chronic mastitis "abnormal involution," but the name did not become popular. Paul Thiele considered the disease a somewhat different process which he termed "fibro-epithelial degeneration." Aschoff called it a dysplastic condition. Lukowsky and Berthels, Lexer and Dietrich considered that the primary fibrosis of the breast may have an involutional significance. The idea of an abnormal involution following lactation is also suggested by McFarland in his treatise on residual lactation acini.

The most specific of the views of this group was advanced by Bloodgood, who called the disease "senile parenchymatous hypertrophy," thereby emphasizing that the essential process or at least that with the greatest potentiality was the increased activity of the glandular elements. It is the histologic conception which most closely coincides with the studies of the present paper. Bloodgood even suggested that the intoxicant productive of subjective symptoms in the menopause might be operative in producing the structural changes in the breast.

It is obvious from this discussion that an involutional element in the production of "chronic mastitis" is not incompatible with the truth of either the stasis or hormonal theory.

(4) Endocrine Theory. That Bloodgood believed that the menopausal intoxication might have an effect on the breast has already been noted. In 1919, Pribram, in a purely theoretical article, suggested that

during the involutional process, after many cells had become senile, a few remaining youthful ones still capable of response would proliferate unimpaired under ovarian excitation. Bartlett and Miller have in this country made certain clinical observations on the occurrence of benign hypertrophies of the breast in association with pelvic pathologic processes. Dietrich and Kueckens also have written in favor of the view that abnormal proliferation of the breast tissue is related to irregular ovarian activity, particularly during the involutional period.

The chief proponent of the ovarian theory of origin of abnormal hypertrophies of the breast has, however, been Moszkowicz, whose studies and those of his predecessors on the histology of the menstrual cycle in the breast have already been discussed. From this point Moszkowicz turned to the consideration of the less circumscribed breast lumps that are tender at menstruation. The histology of these lumps was found to be a hyperplasia of the gland fields, an excessive response to the premenstrual stimulation. Transitional forms were then noted between these hyperplasias and the fully developed fibro-adenoma which caused Moszkowicz to assign to the latter a similar origin (fig 3). According to the same author, the changes observable in glands with "chronic mastitis" consist in an untimely hyperplasia of all the elements caused by an ovarian dysfunction and quite analogous to the hyperplastic changes in the endometrium. Moszkowicz considered carcinoma to be the result of the same type of stimulation, chiefly, apparently, because of the association of this disease with the benign conditions (fig 4). The ultimate causes of tumor growth that affect the breast through the sexual organs are probably varied and may include such conditions as constitutional inferiority of the sex glands, toxic injury to the sex glands, endocrine disease and sexual irregularities. Moszkowicz cites little proof of his theories, does not analyze his clinical material to any extent, seems unduly mechanistic in the finer details of his theory and entirely hypothetical in his list of underlying causes. Yet the theoretical possibilities of abnormal growth in the breast in response to ovarian stimuli, as he has suggested it, and particularly with regard to the close parallel with conditions as found in the endometrium, appear quite sound.

(C) *Carcinoma*—The theories of the cause of cancer in the breast have followed closely those for the benign conditions especially those for the diffuse process, because few observers of "chronic mastitis" have failed to find evidence of associated carcinoma and so have provisionally extended their theory to include the malignant forms. Hence the theories of the origin of cancer may be for convenience divided in the same manner.

(1) Carcinoma derived from sweat gland cells, the result of malformation. This view again is chiefly supported by Krompecher.



Fig 3—Transition from glandular hyperplasia to fibro-adenoma (After Moszkowicz Arch f klin Chr, Berlin [Julius Springer] **144** 138, 1927)



Fig 4—Cystadenoma and fibro-adenoma with cysts filled by proliferating epithelium and exhibiting an early stage of malignant transformation (After Moszkowicz Arch f klin Chr, Berlin [Julius Springer] **144** 138, 1927)

(2) Carcinoma as the result of irritants from stasis of secretion. As supporters of this view are once more Adair and Bagg, Keynes, Berthels and Lukowsky.

(3) Carcinoma incidental to certain involutional changes. This point of view has recently been discussed by Oertel in connection with premenstrual changes in both breast and prostate.

(4) Carcinoma from ovarian dysfunction. The early views of Beatson on the subject, the evidence from animal experimentation, the theoretical concepts of Pribram and Moszkowicz have been discussed.

The attack on the problem of cancer of the human breast has been from two different points.

(1) The Histologic. Here the case rests on the evidence of a multitude of authors who have described the pathologic association of cancer and chronic mastitis and the fineness of the histologic boundary between the two (see Tietze, Berthels, Lukowsky, MacCarty, Reclus, Schimmelbusch, Keynes, Ewing, Oertel, Fischer and others). The association in all probability indicates either that the carcinoma is the derivative of the chronic mastitis or that the two are varying expressions of a similar process with a related cause.

(2) The Statistical. The static picture afforded by microscopic preparations can scarcely be hoped to afford proof of the nature of the relations of the benign to the malignant growths. Attempts at production of cancer in man under predetermined conditions are not possible. The ultimate understanding of the origin of cancer must therefore result from a study beginning with the patient with cancer and attempting to sort out from the multitude of innocuous stimuli which her breast has received, the specific ones, if there are such that produced the cancer.

What seems to be the most careful etiologic study yet executed in a series of cases of cancer of the breast was published in 1926 by Dr Janet Lane-Clayton. This work was based on the histories of 508 cases of cancer and 509 noncancerous controls obtained by a group of eight observers in several English and Scottish hospitals. The opportunity thus afforded for collectively obtaining a large amount of accurate material produced a report that must claim precedence over most if not all previous work and which is distinctly discouraging to individual effort.

The most important result of Dr Lane-Clayton's studies appears to be the definite proof of higher relative incidence in nulliparous women. From this fact and from a short discussion of histology, the author draws the cautious conclusion that the continually recurring changes of the menstrual cycle—whatever their precise nature—have an important bearing on the whole process of hyperplasia and carcinoma. At least

she says that her statistics point decidedly against the belief that cancer is more liable to occur in women whose breasts have been used for suckling at repeated pregnancies or in those who have been subject to abscess or suppuration in the course of lactation

The following study cannot be compared with the just discussed report for magnitude or for detailed statistical analysis. It is hoped, however, that a little may be accomplished by approaching the problem from a considerably different angle, particularly by more completely individualizing the cases so that the development of cancer can be studied in relation to the state of the breast at the time of the appearance of the tumor rather than in relation to antecedent behavior or injuries

*(To be Concluded)*



# OSTEOGENIC SARCOMA OF THE HUMERUS

## REVIEW OF THE LITERATURE AND CASE REPORT<sup>†</sup>

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A case of telangiectatic sarcoma of the humerus seen recently at the University of Virginia Hospital presents several features that seem sufficiently interesting to warrant a report. It has been submitted to the Registry of Bone Sarcoma for study. Because the case illustrates certain aspects of the disease mentioned by Ewing, Kolodny and others, a brief summary of the recent literature dealing with osteogenic sarcoma will be made.

### REPORT OF CASE

*History*—R. M., a mulatto boy, aged 17, was admitted to the University of Virginia Hospital on Jan 14, 1929. The family and past history was entirely negative. The chief complaint was enlargement of the left shoulder of one week's duration. Because of slight soreness, which had increased gradually, his attention had been attracted to the shoulder about three weeks prior to the time of his admission. Motion in the joint had been slightly limited because of pain. No enlargement or other change in the appearance of the part had been noticed, however, until the end of the second week. At that time swelling became apparent, and subsequently the shoulder increased in size rather rapidly.

There had been no fever, chills, sweats or other systemic complaints or symptoms. No history of any injury or trauma to the shoulder was elicited.

*Examination*—Examination revealed a well nourished and fully developed colored boy (fig 1). The temperature was 101 F, the pulse rate 100 and respirations 20. The systolic blood pressure was 128 and the diastolic 80. Physically, he seemed entirely normal except for the left shoulder. It was moderately enlarged and had a slightly fusiform appearance because of swelling of the anterior and lateral aspects of the region, which decreased in size as it extended downward toward the anterior axillary fold (fig 1B). The skin was shiny, and tense over the mass, and there was some increase in the local temperature. Palpation of the mass caused pain, and there was slight pitting with pressure. There was a definite feeling of fluctuation in the deeper structures. Motion of the arm at the shoulder was moderately limited because of the pain which attended both active and passive movement of the joint.

Examination of the urine revealed no abnormality. The hemoglobin was 85 per cent, the red cells numbered 4,580,000, and the leukocytes, 11,400. The smear and differential count were normal. The Wassermann reaction was negative and no growth was obtained from a blood culture. Roentgenograms of the chest showed nothing abnormal. Stereoscopic roentgenograms of the left shoulder

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<sup>†</sup> Submitted for publication Feb 7, 1930.

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revealed a moth-eaten area of destruction of the shaft of the left humerus extending from the region of the epiphyseal line downward for a distance of about 8 cm. There were some detachment and bulging of the periosteum of that area. On the lateral aspect there was a fine, threadlike area of increased density about 2.5 cm in length projecting outward and slightly upward from a point of attachment in the region slightly distal to the epiphyseal line (fig 2). The roentgenologic diagnosis was "probable osteogenic sarcoma of the left humerus." The possibility of chronic, low-grade osteomyelitis, however, could not be excluded entirely. Roentgenograms of the remainder of the skeleton showed no abnormality.

The mass was explored with an aspirating needle, and about 10 cc of bloody, serous fluid was recovered from what appeared to be a multilocular cavity, in the walls of which there seemed to be a deposition of calcareous material. Smears and cultures of the fluid failed to reveal either organisms or tumor cells. A guinea-pig, into which injections of some of the material were made, showed no evidence of tuberculosis after six weeks. A biopsy was made on January 21. The pathologic diagnosis made from the tissue was "osteogenic sarcoma, telangiectatic with peritheliomatous arrangement of the cells."



Fig 1—Patient at the time of admission. *A*, only slight enlargement of the left shoulder. *B*, lateral aspect of the shoulder.

*Treatment*—Treatment with Coley's mixed toxins was initiated on January 29. One-fourth minim (0.015 cc) was given for the first dose, and each time the amount was increased until 35 minims (0.21 cc) was reached. The first injections were given intramuscularly, subsequent doses, directly into the tumor. The average rise of the temperature following the injections was to 104 F, and the highest, to 106 F. The injections were discontinued on February 15, after fifteen injections, because of continuous elevation of the patient's temperature and his precarious physical condition.

*Course*—The course of the disease was extremely rapid (fig 3). One month after the patient's admission to the hospital the mass had tripled in size, the hemoglobin was 55 per cent and the red blood cells numbered 3,620,000 (fig 4). Two months after his admission, the mass was more than 35 cm in diameter, the hemoglobin was only 35 per cent and the red cells numbered 2,500,000 (fig 5). At that time the tumor began to break down and became a fungating necrotic mass. Handfuls of necrotic tissue sloughed from the interior of the tumor on several occasions. On March 28 and April 1, several hemorrhages occurred. On April 1, death ensued within a few hours of a severe hemorrhage.

*Necropsy*—Postmortem examination revealed the necrotic tumor mass already described. There was a pathologic fracture of the surgical neck of the humerus.



Fig 2—Roentgenogram of the left shoulder at the time of admission

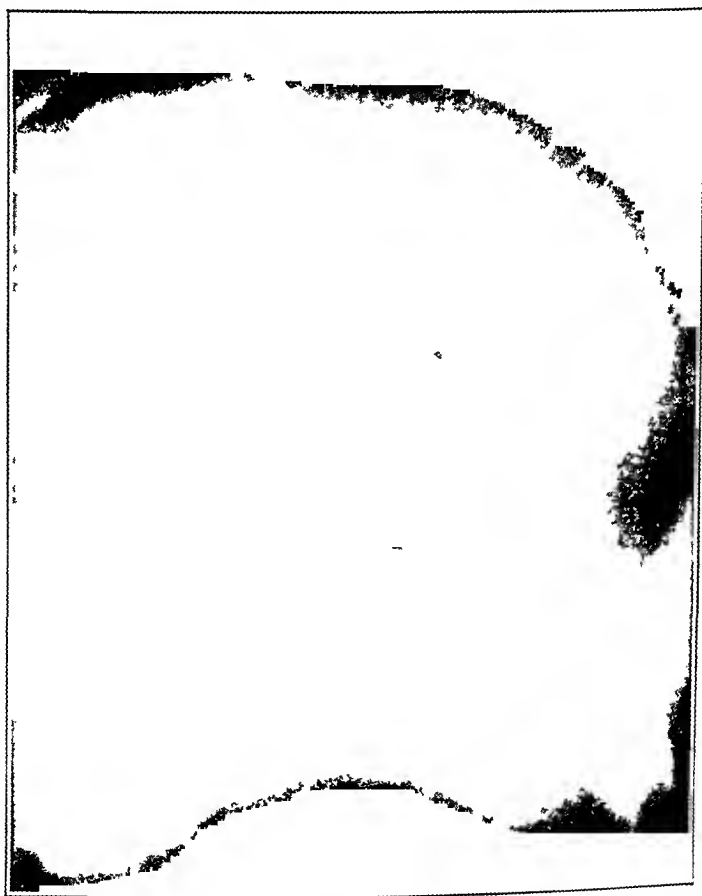


Fig 3—Roentgenogram of the left shoulder one month after admission

(fig 6) Except for a small metastatic nodule about 1 cm in diameter in the lower part of the upper lobe of the left lung, no evidence of metastasis of the growth was found. No other positive observations were made.

#### REVIEW OF THE LITERATURE

Prior to 1920, when the Registry of Bone Sarcoma was organized by Codman through the American College of Surgeons, there was widespread misunderstanding in regard to the classification, pathology, clinical course, prognosis, diagnosis and treatment of tumors of the bone. In 1920 Kolodny stated that the diagnosis was erroneous in one half of all cases diagnosed as sarcoma of the bone by the clinician and pathologist.



Fig 4—Anterior and lateral views of the shoulder one month after admission.

Since that time certain aspects of the subject have been greatly clarified by intensive study of the material of the Registry. Notable contributions have been made by Bloodgood,<sup>1</sup> Christensen,<sup>2</sup> Codman,<sup>3</sup> Ewing,<sup>4</sup>

1 Bloodgood, J. C. How to Diagnose and Treat a Bone Lesion, *J. Bone & Joint Surg.* 8:470 and 727, 1926, 9:217, 1927.

2 Christensen, F. C. Bone Tumors. Analysis of 1,000 Cases with Special Reference to Location, Age and Sex, *Ann. Surg.* 81:1074, 1925.

3 Codman, E. A. The Registry of Cases of Bone Sarcoma, *Surg. Gynec. Obst.* 34:335, 1922, Registry of Bone Sarcoma. I. Twenty-Five Criteria for Establishing the Diagnosis of Osteogenic Sarcoma, II. Thirteen Registered Cases of "Five-Year Cures" Analyzed According to These Criteria, *Surg. Gynec. Obst.* 42:381, 1926.

4 Ewing, J. Neoplastic Diseases, ed. 3. Philadelphia, W. B. Saunders Company, 1928, p. 1127.

Kolodny<sup>5</sup> and others Kolodny's monograph is classic It represents a comprehensive personal study of 700 cases of the Registry and an extensive review of the literature

*Incidence*—Christensen analyzed 1,000 cases of tumors of the bone assembled from the Registry and certain other sources He studied



Fig 5 Anterior and lateral views of the shoulder two months after admission Note the great vascularity of the skin and the fungation of the tumor at the site of the biopsy

the material particularly with reference to the location of the tumors and the age and sex of the patients He found that the most frequent

<sup>5</sup> Kolodny, A Bone Sarcoma The Primary Malignant Tumors of Bone and the Giant Cell Tumor, Surg Gynec Obst 44 214 (April) 1927

site of osteogenic tumors, both benign and malignant, was at the ends of the long bones where there is an epiphyseal disk of maximum growth, where the growth period is longest and where the growth momentum is greatest. Of osteogenic sarcomas, 58.7 per cent were in males and 41.3 per cent in females. Osteogenic sarcoma occurred oftenest in the second decade of life, reaching a maximum incidence at the age of 15 years. At no period of life, however, was there complete immunity.

Of all sarcomas one in three was osteogenic, and the knee was the most frequently involved part of the body. Fifty-two per cent of oste-



Fig 6—The tumor at the time of necropsy. Note the upper end of the humerus lying free in the tumor, which had become necrotic and sloughed extensively.

ogenic sarcomas occurred in the femur, 20 per cent in the tibia and 9 per cent in the humerus. The remaining 19 per cent were distributed among the other bones of the body. It is interesting that no case of osteogenic sarcoma of the lower end of either the radius or the tibia has occurred in the material of the Registry.

*Etiology*—Intensive study has failed to throw much light on the etiology of osteogenic sarcomas. Kolodny mentioned the gradations of cases from those with tissue not unlike callus to those with very cellular tissues. He suggested that the development of osteogenic sarcoma is

probably guided by the same principal laws of growth that are usually observed in the animal organism when in the stage of natural growth or when repair and regeneration take place. Some unknown stimulus breaks the "growth restraint." Trauma has frequently been suggested as such a stimulus. In a recent paper, Knox<sup>6</sup> made a study of trauma in relation to tumor formation and concluded that a single trauma had rarely if ever been proved conclusively to be of etiologic significance.

*Classification*—The term "osteogenic" (Ewing) indicates that the tumor has arisen from cells the function of which it is to form bone but which may or may not do so. When bone is actually formed, the tumor may be still further qualified as "osteogenetic." The following classification of tumors of the bone was adopted by the Registry as a basis for study:

- 1 Metastatic tumors primary in tissues other than bone
- 2 Periosteal fibrosarcoma
- 3 Osteogenic tumors
  - (a) Benign
  - (b) Malignant
- I Periosteal
- II Medullary and subperiosteal
- III Sclerosing
- IV Telangiectatic
  - 4 Inflammatory conditions
  - 5 Benign giant cell tumors
  - 6 Angiomas
    - (a) Benign
    - (b) Malignant
  - 7 Ewing's tumor
  - 8 Myeloma

Kolodny discussed this classification and pointed out certain insufficiencies in it. He mentioned the importance of classification according to cell origin rather than cell type for in the same tumor different areas may show many different structures, such as fibrosarcoma, cartilage or bone. He suggested that until more accurate data were available all primary malignant bone tumors be subdivided into four groups:

- 1 Osteogenic sarcoma
- 2 Ewing's sarcoma
- 3 Myeloma
- 4 Unclassified sarcoma including angio-endothelioma and extraperiosteal sarcoma

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6 Knox, L. C. Trauma and Tumors, Arch. Path. 7: 274 (Feb.) 1929

*Pathology*—Kolodny characterized osteogenic sarcoma as a tumor derived from cells that are descendants of mesoblastic elements predestined embryologically to form bone. Hence these cells have the potential ability to differentiate into osteoblasts. In the differentiation there are many intermediate stages and therefore many different structures in the same or different tumors.

The commonest cell type in osteogenic sarcoma is the spindle cell, usually the small variety with a hyperchromatic nucleus. The epulis type of giant cell and the round cell are no longer classed among those found in sarcoma of the bone. The chief morphologic difference between osteogenic sarcoma and other malignant tumors is its intercellular substance, which may be hyaline, osteoid, cartilaginous, myxomatous or osseous.

Spontaneous lymphocytic infiltration in the absence of previous biopsy or treatment seems to indicate some defense reaction to the tumor on the part of the body. All of the Registry cases of five year cures showed this phenomenon, but not all cases that showed it were cured for five years.

*Clinical Course and Prognosis*—The onset may be and frequently is insidious. In the early stages of the disease many patients have been treated for rheumatism because of pain in the region of a joint. The tumor may not become apparent for some time. The rapidity with which it grows usually depends on the degree of its malignancy. The prognosis, while apparently poor in all cases, depends on the degree of malignancy of the tumor. In 1922, one and one-half years after the Registry was instituted, Codman stated: "We know of only four cases of true osteogenic sarcoma which are alive in this country today, who were treated over five years ago. These were treated by amputation alone." In 1926, he analyzed thirteen "five-year cures" and stated that in the majority of these cases some doubt as to the certainty of the diagnosis had been expressed by some of the reviewing pathologists.

*Diagnosis*—According to Ewing, persistent, increasing and unexplained pain is the most significant and the earliest symptom in nearly all cases. This is apparently due to the stretching of the sensitive periosteum by the growing tumor. It calls for the provisional diagnosis of osteogenic sarcoma at once. The general health of the patients is nearly always good. More or less fixation of the soft parts and increase in the venous circulation of the skin are observed early in most cases. Some local heat and a slight elevation of body temperature are not uncommon.

The roentgenogram is of the greatest diagnostic importance. Its chief features are roughening of the outer surface of the shaft and lifting of the periosteum at the advancing edge of the tumor, the "reactive triangle" of Codman.



Biopsy may be employed as a diagnostic aid in certain cases Goodwin,<sup>7</sup> in discussing tumors of the bone, recognized three types of cases diagnostically. In one group were those in which the diagnosis of malignancy was apparent, in another those in which the evidences of benignity were certain. In between these were borderline cases in which the history, the physical observations and the roentgenograms were not conclusive, cases in which accurate differentiation between a benign and a malignant lesion was most important in order to decide between conservative and radical treatment. He stated that only in this group of cases does biopsy serve a useful purpose. In the other groups it is usually unnecessary. Furthermore, a biopsy made merely as a matter of record in inoperable cases is unfair to the patient because of the consequent stimulation to tumor growth and the subsequent fungation of the tumor which is almost certain to follow this procedure, thereby adding to the misery of the patient until he is relieved by death. When resorted to, biopsy must be done between tourniquets to prevent dissemination of malignant cells. If the tissue proves malignant, immediate amputation is indicated.

*Treatment*—Ewing characterized the treatment for osteogenic sarcoma as "a difficult and complex subject calling for skill and experience." Its results are unsatisfactory. These tumors resist irradiation and become more painful and somewhat swollen before the resulting slow regression sets in. Preliminary irradiation as a therapeutic test and as a preoperative measure is thought worth while by Ewing. He stated that he was unable to evaluate the effects of Coley's<sup>8</sup> toxins in cases of osteogenic sarcoma. Codman expressed the belief that amputation plus Coley's toxins offers the best chance of cure.

*Telangiectatic Group*—The telangiectatic variety of osteogenic sarcoma presents certain special features of interest in connection with the case reported.

As the name implies, this is a very vascular tumor. The vessels may be so large and numerous that the tumor pulsates, giving rise to the term "malignant bone aneurysm." Such tumors develop very rapidly, destroy the shaft early with resulting pathologic fractures and yield metastases with a fatal termination within a few months. The growth is usually composed of a series of communicating blood sinuses lined by hyperchromatic spindle and polyhedral cells and supported by strands of partly ossified tumor tissue. The periosteum is soon perforated, and the tumor

<sup>7</sup> Goodwin, W. H. Tumors of the Bone. A Comparative Study, Arch Surg **18** 2353 (June) 1929.

<sup>8</sup> Coley, W. B. The Differential Diagnosis of Sarcoma of the Long Bone. I Bone & Joint Surg **10** 420 1928.

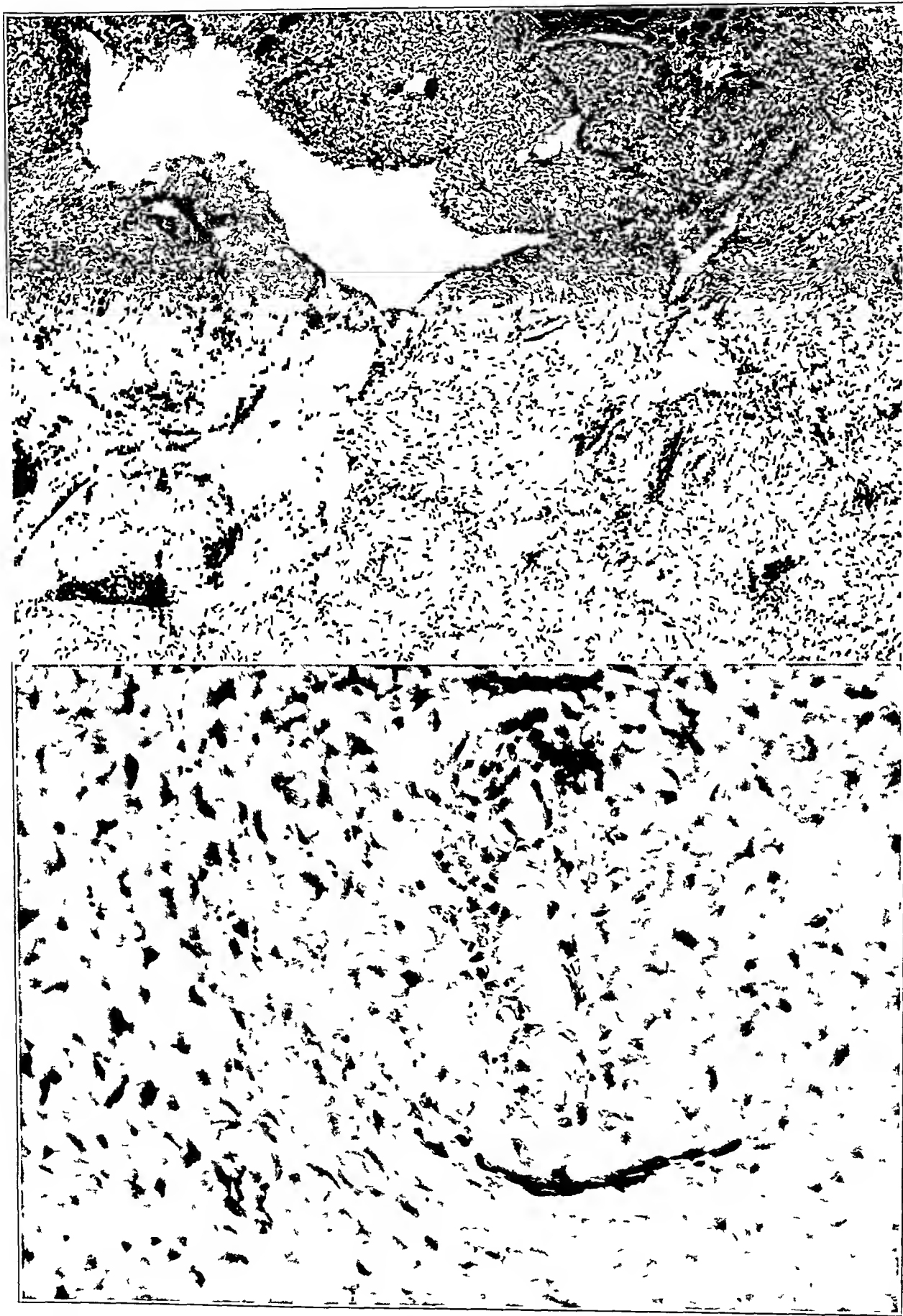


Fig 7—Section of the tumor (biopsy) The upper part has a magnification of 50, the lower, 300

sinuses ramify through the muscles or into the joint. A considerable segment of the diaphysis may be found free in the center of the blood mass.

Except in the early stages the roentgenogram fails to reveal the usual features of osteogenic sarcoma. The elevation of the periosteum is soon obscured by the complete destruction of the shaft of the bone and the periosteum. Such tumors progress very rapidly, and a serious condition is reached within a few weeks. These tumors carry the worst prognosis of any group and Ewing said that as far as he could learn all cases of this form of sarcoma have proved fatal.

#### COMMENT

The most outstanding clinical features of this case were the extreme rapidity of growth of the tumor and the immense size attained by it. Only four months elapsed between the time of the onset of the first symptoms and the death of the patient. In spite of the rapid growth and great malignancy of the tumor, however, only one metastatic tumor was found at necropsy.

The age of the patient corresponds closely to that of the maximum incidence of the disease as given by Christensen. There was no history of antecedent trauma and no other apparent etiologic factor was discovered.

The influence of the biopsy on the course of the disease is difficult to determine with assurance. The tumor had already broken through the periosteum and invaded the muscles of the arm when the biopsy was made. It is certain, however, that the biopsy must have been directly responsible for the early fungation of the tumor. In view of the many vascular channels that must have been made accessible to detached tumor cells at the time of the biopsy, it seems remarkable that no more than one metastatic tumor was found at necropsy. The small size of this nodule suggests implantation at a much later time than that of the biopsy when the rapidity of growth of the mother tumor is considered.

The structure of the tumor illustrates the point made by Kolodny that different areas of the same tumor frequently show many different structural characteristics. In this case the tissue removed at biopsy was typically telangiectatic, while sections from other portions of the tumor taken at necropsy revealed various different structural characteristics (figs 7, 8 and 9).

The diagnosis presented an interesting problem. The relatively acute onset, the pain, tenderness, swelling, local heat and fluctuation, the elevation of the patient's temperature and the number of leukocytes suggested the possibility of a low-grade osteomyelitis of the humerus. Even the roentgenogram showed some of the features commonly found in osteomyelitis.

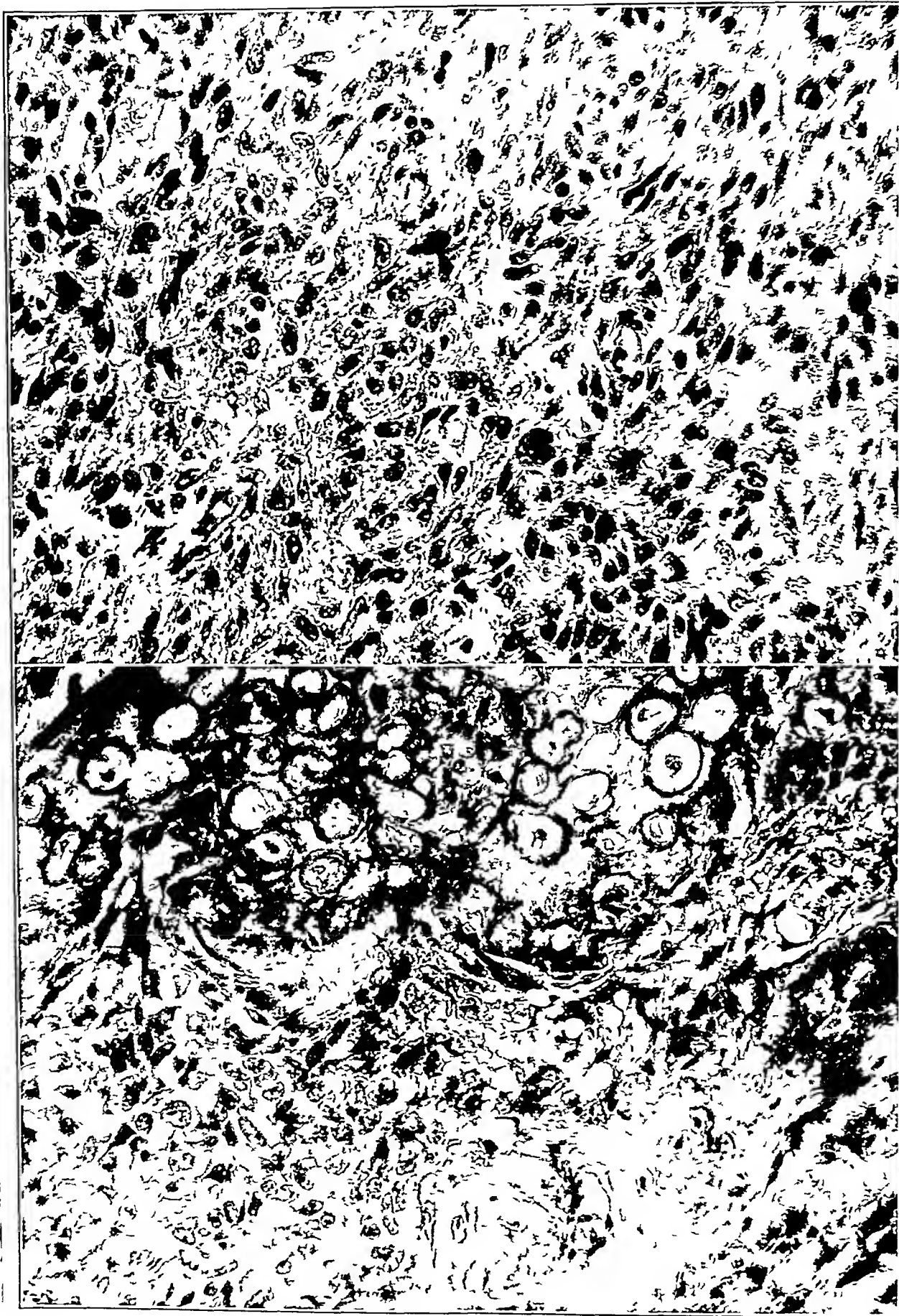


Fig 8—Sections of the tumor (necropsy),  $\times 300$

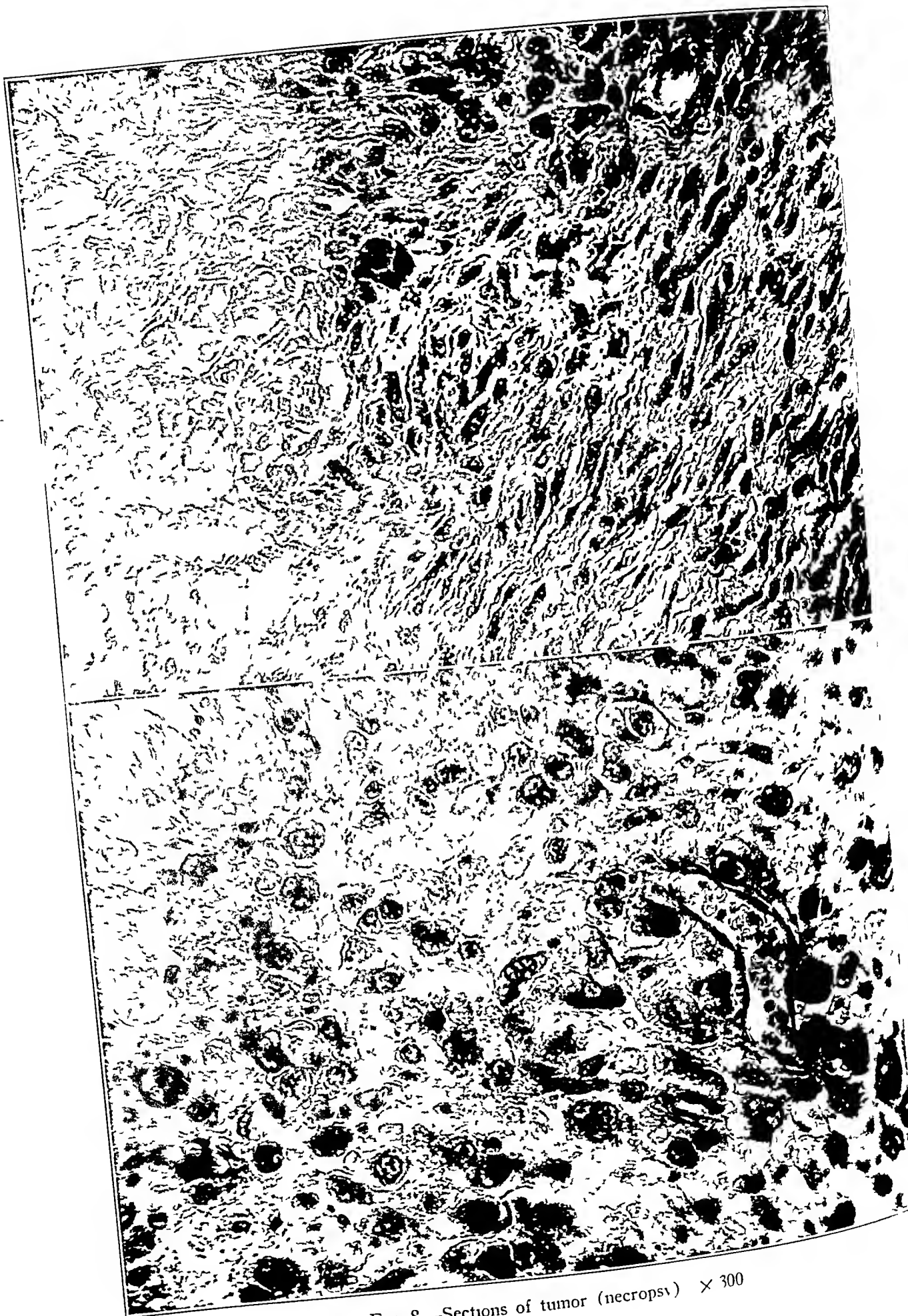


Fig 8—Sections of tumor (necropsy)  $\times 300$



The course of the disease and the fact that only one small metastatic tumor was found at necropsy cause one to regret that the patient was not given the chance, poor though it might be, offered by a shoulder-girdle amputation. Such an excision of the tumor would have almost certainly prolonged the patient's life and at least saved him from the discomforts caused by the local growth. Coley's toxins did not seem to be of any value in this case.

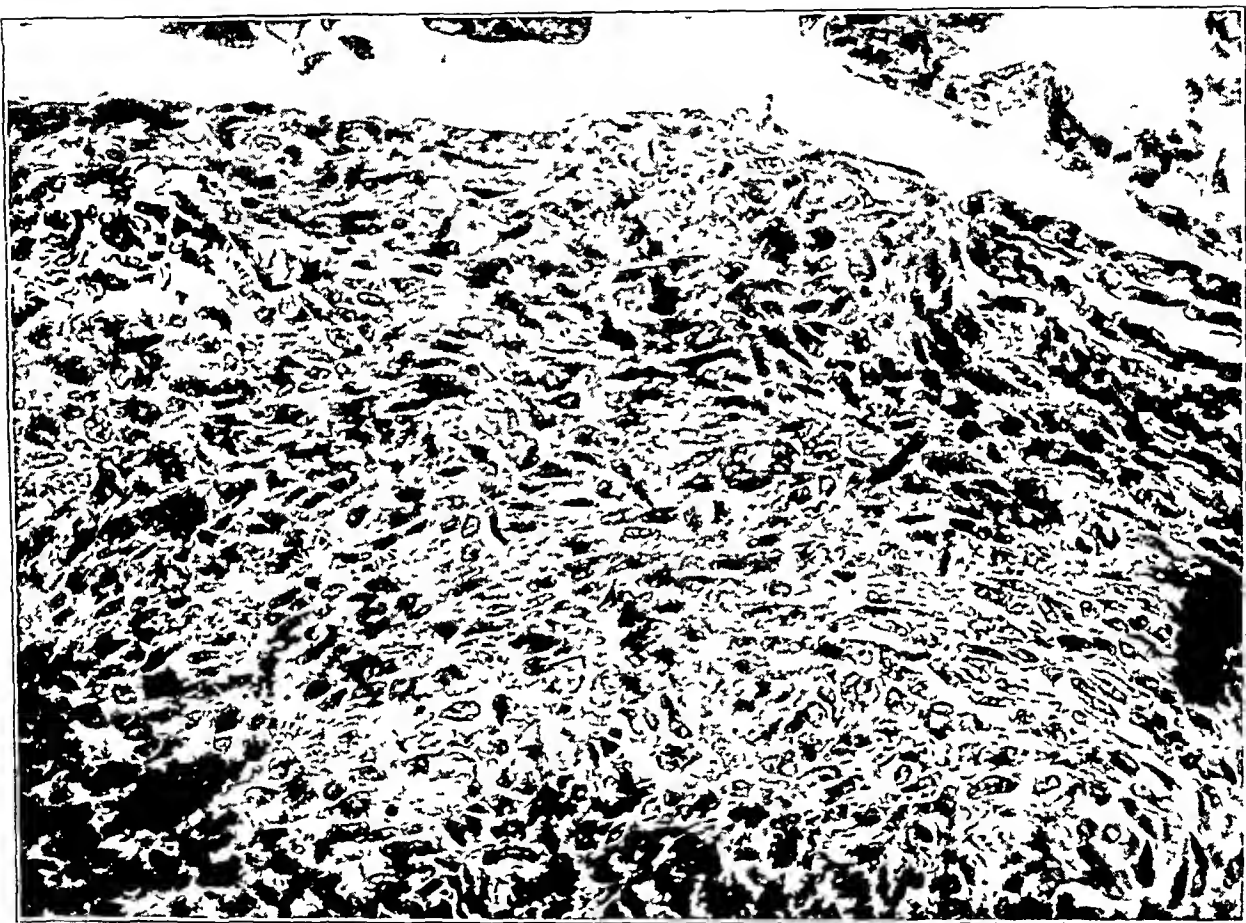


Fig 9—Section of metastatic tumor in the lung,  $\times 300$

#### SUMMARY

The history of a case of telangiectatic osteogenic sarcoma of the humerus is presented and a brief resumé made of the recent literature on osteogenic sarcoma. The most outstanding features of the case were the extreme rapidity of growth of the tumor and the immense size attained by it. Only four months elapsed between the time of the onset of the first symptoms and the death of the patient. The case is discussed briefly from the standpoint of the pathology, diagnosis and treatment.

# URETEROCELE \*

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Ureterocele, one of the less common abnormalities of the genitourinary tract, is the intravesical bulging of the mucosa of the lower end of the ureter. Kaufmann stated <sup>1</sup> "If a ureter ends blindly at its vesical end, or if the vesical end of one or both ureters narrows down to an exceedingly fine opening, the end of the ureter covered with vesical mucosa bulges into the bladder like a bubble or cyst, ureterocele vesicalis." Ureteroceles appear as rounded protrusions at one or both ureteral orifices, and, before the days of cystoscopy, they were discovered only post mortem or accidentally in the course of intravesical operations.

## DISCUSSIONS IN THE LITERATURE

*Historical Observations*—Most of the early observations were made at necropsy, the earliest, according to Patch,<sup>2</sup> by Lechler,<sup>3</sup> in 1835. Civiale<sup>4</sup> mentioned cystic dilatation of the ureter in 1843. Lihlenfeld<sup>5</sup> described the first pathologic specimen of the kind in 1856, and in 1862, Smith<sup>6</sup> reported observations on a specimen in which there was bilateral ureterocele. Until 1898, Englisch<sup>7</sup> was able to collect only sixteen authentic cases, and in 1906, Adrian<sup>8</sup> reported fifty-two cases from the literature, mostly accounts of specimens obtained at necropsy.

Apparently the earliest operative intervention for correction of the condition was by Streubel,<sup>9</sup> in 1858. The first excision of ureterocele

\* Submitted for publication, Aug 29, 1929

\* From the service of Waltman Walters, Division of Surgery, The Mayo Clinic

1 Kaufmann, Edward. Pathology for Students and Practitioners, Philadelphia, P. Blakiston's Son & Company, 1929, vol 3, pp 2224

2 Patch, F S. Ureterocele, with Report of a Case, J Urol **16** 125, 1926

3 Lechler, quoted by Patch. J Urol **16** 125, 1926

4 Civiale, quoted by Kreissl and Gehl. Illinois M J **37** 315, 1920

5 Lihlenfeld, quoted by Lavandera. Surg Gynec Obst **32** 139, 1921

6 Smith T. Prolapsus of Ureters into Bladder, Tr Path Soc London **14** 185 1862

7 Englisch, J. Ueber cystenartige Erweiterung des Blasenendes des Harnleiters, Centralbl f d Krankh d Harn- u Sex-Org **9** 373, 1898

8 Adrian, C. Ein neuer operativ behandelter Fall von intermittirender cystischer Dilatation des vesicalen Ureterendes, Arch f klin Chir **78** 588 1906

9 Streubel quoted by Patch. J Urol **16** 125, 1926

by suprapubic exposure was by Freyer<sup>10</sup> in 1898. In 1903, Fenwick<sup>11</sup> performed the first transurethral operation for excision of ureterocele, and Kelly,<sup>12</sup> in 1906, effected a cure by endovesical excision.

*Nomenclature*—The nomenclature relative to the condition is most confusing, many terms are used, some of which obviously are inaccurate. Terms encountered in the literature are cystic dilatation of the lower end of the ureter, cyst of the lower end of the ureteral tube, ureterovesical cyst, cystocele, prolapse of the vesical end of the ureter, prolapse of the ureter, ballooning of the ureteric orifices, ureterocele and vesical ureterocele. Of these, only the last two are considered to be free from serious objections, and Petillo,<sup>13</sup> in a recent discussion, concluded that ureterocele is the best term.

*Etiology*—Early reports indicated that ureterocele was more common in young females. It has since become apparent, however, that the condition is found at all ages; the extremes of the ages reported are 4 days and 62 years. The literature seems to indicate that the abnormality is more common in females, although Patch stated that it occurs about equally in the two sexes. In a series of sixteen cases reported by Englisch in 1898, ten were in females, in 1913, Caulk<sup>14</sup> reported six cases, five of which were in females, Martius,<sup>15</sup> in 1927, said "The condition occurs almost twice as frequently in women as in men." The more recent literature contains many reports of the condition in males, practically all of them adults.

The opinion that ureterocele is based on a congenital abnormality is championed by most of the older and many present-day writers. Papin<sup>16</sup> was convinced that the condition could not be acquired. Of thirteen cases reported by Blumer,<sup>17</sup> ten were evidently of congenital origin. Fenwick believed the condition to be dependent on the congenitally blind termination or narrow stricture of the ureteral orifice, and

10 Freyer, P. J. Obscure Cystic Tumour of the Bladder Containing Two Calculi. Successful Removal by Supra-Pubic Cystotomy, Tr. Roy. Med. & Chir. Soc. **81** 41, 1898.

11 Fenwick quoted by Michel. Urol. & Cutan. Rev. **25** 726, 1921.

12 Kelly, H. A. Two Cases of Stricture of the Ureter, Two Cases of Hydronephrotic Renal Pelvis Successfully Treated by Plication, Bull. Johns Hopkins Hosp. **17** 173, 1906.

13 Petillo, Diomedeo. Ureterocele. Clinical Significance and Process of Formation, Surg. Gynec. Obst. **40** 811, 1925.

14 Caulk, J. R. Ureterovesical Cysts. An Operative Procedure for Their Relief, J. A. M. A. **61** 1685 (Nov. 8) 1913.

15 Martius, H. Zur Behandlung der Ureterocele vesicalis, Zentralbl. f. Gynäk. **51** 327, 1927.

16 Papin, E. quoted by Patch. J. Urol. **16** 125, 1926.

17 Blumer, G. Notes on Two Cases of Ureteral Abnormality, Bull. Johns Hopkins Hosp. **7** 174, 1896.



that the force from above, transmitted to the mucous membrane covering the blind end, or on the weak intramural ureter above a narrowed orifice, causes it to bulge into the cavity of the bladder in the form of a globular cyst. Michel<sup>18</sup> favored Fenwick's theory, but did not think it necessary that the ureter should have an abnormal course through the wall of the bladder, as suggested by Caulk<sup>19</sup> and Bachrach,<sup>20</sup> or that the muscle of the wall of the bladder should be deficient about the ureter. The dilatation of the ureter occurs, he believed, under the mucosa of the bladder, after it penetrates the muscle. Barringer,<sup>21</sup> in discussing the mode of production of ureterocele, said "It is probable that the stricture of the ureteral opening is always congenital."

Thomas and Mellen<sup>22</sup> pointed to the embryonic development of the ureter in supporting the theory of congenital origin. They assumed that failure of development in the renal bud of sufficient lumen at its lower end, as it joins the bladder, may account for the strictured ureteral orifice, also, that the opening which develops in the lining of the bladder may not be large enough.

Petillo, on the other hand, completely discarded the theory of congenital origin of the condition, and ably defended the idea of the acquired nature of ureterocele. Contrary to most writers, he does not believe that stenosis of the ureteral orifice is the cause of ureterocele; he reasons that if it were the condition would be much more common than it is. In a recent article, he pointed out that a local infection of the lower genito-urinary system, such as seminal vesiculitis, may interfere with the innervation of the vesical end of the ureter, causing nerve block, paralysis and atony, and consequent dilatation of the intramural part of the ureter. Petillo quoted the experimental work of Protopopow to support his theory of local infection as a cause of ureterocele and cited four cases in which ureterocele followed infection of the lower portion of the genito-urinary tract. It is his belief that in the female, pelvic inflammatory conditions could effect the ureter. McKenna,<sup>23</sup> in a paper

18 Michel, L. L. Ureterocele or Cyst of Lower End of Ureter. A Collective Abstract with Report of a Case, *Urol & Cutan Rev* **25** 726, 1921.

19 Caulk, J. R. Description of Two Procedures for the Relief of Obstructions at the Vesical End of the Ureter. Presentation of a High Frequency Cystoscopic Scissor Incisor, *J Urol* **11** 565, 1924.

20 Bachrach, R. Die Erkrankungen der Harnleiter, in von Lichtenberg, A. Voelcker F., and Wildbolz, H. *Handbuch der Urologie*, Berlin, Julius Springer, 1928 vol 5 Spezielle Urologie, p 1.

21 Barringer, B. S. Unilateral Kidney Calculus Complicated by Ureterocele of the Opposite Side, *Interstate M J* **20** 343, 1913.

22 Thomas, G. J., and Mellen, D. H. Bilateral Cystocele or Cystic Dilatation of the Lower End of the Ureters. A Successful Method of Treatment, *Minnesota Med* **4** 475, 1921.

23 McKenna W. F. Ureterocele, *S Clin North America* **7** 1001, 1927.

published two years ago, defended the theory that the condition is acquired, asserting that dilatation may occur above a stricture following local infection. Lavandera<sup>24</sup> expressed the belief that the condition may result from stenosis following injury from a ureteral stone, from tuberculosis or from any inflammatory process of the ureter. He added, however, "The majority are due to a ballooning of the ureter behind a congenitally stenosed orifice."

The supporters of the theory of congenital origin point to the frequent co-existence of ureterocele and manifestly congenital malformations as additional evidence that the condition is not acquired. Patch estimated that ureterocele is associated with congenital anomalies in about 50 per cent of cases. In thirty-two of the sixty-four cases reviewed by Lavandera the condition was accompanied by anomalies of the genito-urinary system, mainly double ureters. Caille's<sup>25</sup> case was that of an infant aged 2 weeks, who had double ureters. Spooner and Lindsey,<sup>26</sup> of the Mayo Clinic, reported a case of multiple malformations seen at necropsy in an infant 4 days old. Bostroem<sup>27</sup> Beach,<sup>28</sup> Ogle<sup>29</sup> and Tangl<sup>30</sup> have reported cases of ureterocele associated with anomalies obviously congenital, including abnormalities of the renal pelvis, and ureters, hypospadias, imperforate anus, cleft palate and harelip.

Champions of the theories of congenital and of acquired origin are agreed that the significant factor is the existence of obstruction at the ureteral meatus. Ureterocele was present in two of the five cases of obstruction at the ureterovesical juncture reported by Mertz<sup>31</sup>. Caulk is of the opinion that the obliquity with which the ureter pierces the

24 Lavandera, M. Further Observations on Ureteroceles, *Surg Gynec Obst* **32** 139, 1921

25 Caille, Augustus. Prolapse of the Inverted Lower Portion of the Right Ureter Through the Urethra in a Child Two Weeks Old, *Am J M Sc* **95** 481, 1888

26 Spooner, C M, and Lindsey, Maude L. Intravesical Ureteral Cyst, Associated with Embryonic Cartilage in the Kidney of a Newborn Infant, *J Urol* **17** 453, 1927

27 Bostroem, E. Beitrage zur pathologischen Anatomie der Nieren, Freiburg i B and Tübingen, J C B Mohr, 1884, part 1, pp 48

28 Beach, Fletcher. Bladder Containing a Pouch Which Opens into a Dilated Coiled Tube (a Third Ureter), Communicating with the Right Kidney by a Smooth Walled Cavity, Which is Shut Off from the Remaining Portion of the Kidney, *Tr Path Soc London* **25** 185, 1874

29 Ogle, Cyril. Dilated Ureter and Pelvis of the Left Kidney, with Prolapse of Ureter into the Bladder, *Tr Path Soc London* **45** 127, 1894

30 Tangl, Franz. Beitrage zur Kenntnis der Bildungsfehler der Urogenitalorgane, *Virchows Arch f path Anat u Physiol* **118** 414, 1889

31 Mertz, H O. Congenital Changes in the Urinary Organs as They Influence Puvria of Infancy and Childhood, *J Urol* **19** 371, 1928

wall of the bladder is a predisposing factor, The presence of calculi at the ureterovesical juncture, and particularly their presence within the ureterocele sac, has led several writers to the opinion that the obstruction due to the stone was the cause of the condition of ureterocele. Smith described a case which seems to indicate that obstruction by a stone cannot in itself be the cause of the condition. Lavandera, maintaining strict neutrality, pointed out that a congenital condition may exist and may remain symptomless until adult life, when inflammatory changes become superimposed. Thus, ureterocele thought to be due to infection or calculus may have been present since birth, the superimposed inflammatory process precipitating the symptoms. Lavandera is of the opinion that "It is more logical to think of a stone secondary to ureterocele, than the reverse."

*Pathology and Associated Pathologic Process*—Although the condition usually is unilateral, it may be present on two sides. Portner,<sup>32</sup> in a series of forty cases, found it bilateral in five. Smith, Burckhart,<sup>33</sup> Rathbun,<sup>34</sup> Aschner<sup>35</sup> and Ryall<sup>36</sup> also reported cases of bilateral ureterocele.

Kaufmann described it as a "bulging into the bladder, like a bubble," and Fenwick described its gross appearance by introducing the word "balloon." The size and shape may vary within wide limits, as pointed out by Patch and others. In early cases there is a small rounded tumor with a broad base, while in the more advanced cases the tumor becomes elongated. The shape varies with the distention, some are described as globular, others as ovoid, triangular or finger-like. The walls of the cyst may be thin, glistening and transparent, or thick, reddened and with dilated vessels coursing over the surface. The position of the ureteral orifice varies. It may be at the usual site, but generally it is eccentrically situated on the side or on the posterior aspect of the tumor. The orifice, however, is almost uniformly constricted.

All authors agree that the wall in ureterocele consists of two layers of mucous membrane, that ureteral mucosa lines the inside, and vesical mucosa the outer surface. The nature of the tissue between these two mucous surfaces is controversial, some report having found muscular tissue and others assert that only fibrous connective tissue is present.

32 Portner, E. Ueber intermittierende cystische Erweiterung des vesicalen Ureterendes, Monatsbl. f. Urol. **9** 296, 1904.

33 Burckhart, quoted by Michel. Urol. & Cutan. Rev. **25** 726, 1921.

34 Rathbun, N. P. Bilateral Diverticula of the Ureter, J. Urol. **18** 347, 1927.

35 Aschner, P. A. Cystic Dilatation of Lower End of Ureters. Internat. J. Surg. **34** 241, 1921.

36 Ryall, E. C. Operative Cystoscopy, St. Louis, C. V. Mosby Company, 1925, p. 10.

Urinary calculi often are associated with the condition, many writers report the presence of one or more stones of varied sizes. Different types of ureteral and renal pathologic changes may exist. Usually there are thin-walled, dilated or tortuous ureters, and dilated renal pelvises, with some degree of hydronephrosis or pyonephrosis. Atrophy of the kidney has been found infrequently. Often some degree of cystitis exists.

*Symptoms*—The symptoms presented in ureterocele vary widely with the size and situation of the tumor, and the presence or absence of infection. As has been stated symptoms may not be present, the condition may be found accidentally. On the other hand, the patient may appear acutely ill, and may suffer severe colicky pain, accompanied by pyrexia and leukocytosis. Many patients with this condition complain of dull, aching pain in the flank, often radiating to the region of the bladder.

Caulk, Hyman<sup>37</sup> and others have classified the symptoms as renal and vesical. The former group are essentially those of obstruction—that is, of hydronephrosis or pyonephrosis and obtain in cases in which the ureteral orifice is obstructed. Instances in which the opposite ureter was obstructed have been reported. Symptoms referable to the bladder may be only those of cystitis, or if the tumor blocks the urethral orifice, the evidences of obstruction to urinary outflow may be added. Furnival's<sup>38</sup> case is interesting. In a girl, aged 16, the first symptom was sudden discharge of blood from, it was thought, the vagina. At first this was considered to be the onset of catamenia. Later, urinary incontinence, frequency and straining appeared, and the tumor, ureterocele by pathologic diagnosis after removal, was seen presenting at the vulva. In many other early accounts cases were described in which the tumor had passed through the female urethra and appeared at the meatus. This had occurred in four of the cases reported by Blumer, the case of Davies-Colley<sup>39</sup> was that of a girl, aged 18 months, in whom the tumor projected from the urethral orifice.

*Diagnosis and Differential Diagnosis*—It is apparent that the diagnosis of ureterocele can be only presumptive save by cystoscopic examination or surgical exploration. There are no pathognomonic symptoms. The tumor may be seen at the usual site of the ureteral orifice extending into the cavity of the bladder. Hyman warns that it may be overlooked,

37 Hyman, Abraham. Ureterocele with Especial Reference to Endovesical Treatment, *Urol & Cutan Rev* **22** 435, 1918.

38 Furnival, F. H. Cystic Dilatation of Lower End of Ureter, *Australasian M Gaz* **23** 394, 1904.

39 Davies-Colley. Specimen of Malformation and Disease of the Ureter and Bladder in a Female Child Eighteen Months of Age, *Lancet* **1** 372, 1879.

especially if it happens to be empty and collapsed. Young<sup>40</sup> vividly described the characteristic intermittent ballooning of the tumor. Hyman, Caulk, Kelly, McKenna and others have also described and emphasized this ballooning as being characteristic of ureterocele.

Prolapse of the lower end of the ureter is the condition from which ureterocele must be carefully distinguished. The size of the ureteral orifice has been mentioned as a significant point in the differential diagnosis. In prolapse the mucosa is turned out through an enlarged orifice, whereas in ureterocele the orifice is small and the mucosa is not everted. Kapsammer<sup>41</sup> observed that in prolapse the blood vessels appear sharply cut off at the base, in a ureterocele the delicate network of vessels can be seen coursing over the cyst. Other points of difference in the two conditions, as seen by Kreissl and Gehl,<sup>42</sup> are as follows. In prolapse the tumor is pedunculated, the top is broad and the ureteral orifice is situated centrally, in ureterocele the base is broad and the orifice is situated eccentrically. In prolapse, the prolapsed mucosa can be replaced in the ureter, whereas this is not possible if the condition is a ureterocele. Thomas and Mellen called attention to the fact that when filled with urine, a ureterocele sac will transmit light as does a hydrocele sac.

The clinical picture of ureterocele may also resemble that of appendicitis, pelvic infection or disease of the gallbladder, as well as other conditions of the urinary tract with which it may be associated. Benign neoplasms of the bladder must also be differentiated from ureterocele.

*Treatment*—The treatment for ureterocele is entirely surgical. In former days suprapubic cystostomy usually was done. The methods of attacking the tumor vary from simple slitting of the cyst, with suture of the two mucous layers, to complete resection and circular suture of the mucosa. Many surgeons still consider the suprapubic route the method of choice, especially in male patients.

According to Patch, the important consideration in the treatment is prevention of ureteral and pelvic stasis. Eisendrath<sup>43</sup> pointed out that the method of treatment must depend on the amount of renal injury and the presence or absence of infection. If the kidney is injured to such an extent that its function is markedly impaired, and if infection is evident, he chooses to do nephrectomy. Resection of the tumor, with

40 Young, H. H. A Case of Intravesical Dilatation or Ballooning of the Ureter, Maryland M. J. **43** 552, 1900.

41 Kapsammer, G. Ueber cystische Erweiterung des unteren Ureterendes, Ztschr. f. Urol. **2** 800, 1908.

42 Kreissl, F., and Gehl, W. H. Concerning Cystic Dilatation of the Vesical End of the Ureter with Report of Case, Illinois M. J. **37** 315, 1920.

43 Eisendrath, D. N. Congenital Stenosis of the Ureter, Surg. Gynec. Obst. **12** 533, 1911.

transplantation of the ureter into the bladder at another point, may be done Harnagel<sup>44</sup> stated that nephrectomy and ureterectomy have been done without disturbing the cyst Macalpine reported a case in which he removed the tumor through the opening made at suprapubic cystostomy, with cure

Many writers have reported excellent results after treating conditions of ureterocele by the transurethral route Fenwick, in 1903, operated successfully through the urethra Kelly Caulk, Wolf,<sup>46</sup> Young Buerger<sup>47</sup> and many others have accomplished clinical cures by endovesical procedures of various types Wolf used the cautery of an operating cystoscope to destroy the tumor, Caulk slit the wall of the cyst with vesical scissors, Young used his cystoscopic rongeur to remove the wall of the sac, Buerger introduced a knife and punch forceps through the cystoscope

Petillo, Martius and Ehrich<sup>48</sup> expressed the opinion that endovesical electro-coagulation is undoubtedly the method of choice Petillo considered suprapubic cystostomy and resection of the ureterocele as surgical abuse, except under extenuating circumstances Aschner, Ryall, Brown,<sup>49</sup> Pollet<sup>50</sup> and others also reported good results following transurethral fulguration, and consider this method of treatment adequate and simple Ehrich considered the only advantage of the suprapubic procedure to be the possibility of doing a bilateral operation in one step

A number of recurrences after transurethral operation have been mentioned in the literature, but it is the opinion of many writers that these could have been prevented by systematic dilatation of the urethral orifice by means of bougies and catheters Thomas and Mellen concluded that in mild types of ureterocele the condition can be cured by repeated dilatation of the ureteral orifice, together with pelvic lavage They emphasize the importance of clearing up all urinary infection, and in their practice, they search for and eradicate all focal infection, such as that of tonsils and teeth

In 1924, Caulk described his "high frequency scissors," which burn as they cut, to relieve obstruction at the ureterovesical juncture Later

44 Harnagel, E J A Simple Treatment of Certain Lesions of the Intra-vesical Ureter in the Female, *J Urol* **10** 141, 1923

45 Macalpine, J B Case of Ureterocele, *Proc Roy Soc Med (Sect Urol)* **15** 35, 1921-1922

46 Wolf, L, quoted by Kreissl and Gehl *Illinois M J* **37** 315, 1920

47 Buerger, Leo Ureteral Obstruction, *New York M J* **105** 909, 1917

48 Ehrich, E Zur Behandlung der Ureterocele, *Zentralbl f Chir* **54** 3212, 1927

49 Brown, D A Ureterocele, *J Urol* **16** 363, 1926

50 Pollet Cystic Dilatation of Lower End of Ureter, *J d'urol* **11** 15, 1921, abstr, *J A M A* **76** 1324 (May 7) 1921

in the same year, Bumpus<sup>51</sup> described a ureteral scissors designed to cut obstruction at the ureteral orifice, under guidance of the eye

In 1924, Romaine<sup>52</sup> reported a case in which treatment was by suprapubic cystostomy and excision of a large ureterocele, and in which cure was brought about. He advised against transurethral fulguration for the following reasons. Repeated fulguration would have been necessary, the danger of ulceration of the wall of the bladder was thought to be too great, he feared possible scar formation, with stricture and serious injury to the kidney. Another danger of transurethral operation, as brought out in the literature, is that of postoperative hemorrhage. No such accidents of consequence have been reported, however. Martius warned against intravesical fulguration of the two sides at one operation, because of the temporary interference with the passage of urine that may follow. Ehrlich expressed the belief that such procedures must be done in two steps, because obstruction is relieved only after the necrotic eschar has detached itself.

Blum<sup>53</sup> cited a case of ureterocele in which there was a calculus in the sac, and in which the sac ruptured spontaneously, with clinical cure.

This review of the literature was stimulated by two cases in which operation was recently performed at the Mayo Clinic by Walters.

#### REPORT OF CASES

CASE 1—The patient was a nulliparous, married woman, aged 25, who had always been well, except for some urinary frequency, until eleven months prior to her visit to the clinic. She then had an attack of severe colicky pain in the suprapubic region, it did not radiate, and was accompanied by nausea, but not dysuria.

When the urine was examined it was reported to contain a great deal of pus, the pyuria persisted during the intervening eleven months. Nothing of significance was discovered on general examination. Urinalysis revealed red blood cells graded 1 and pus graded 4. Tests of renal function showed the right kidney to be functionless. The concentration of urea was estimated at 20 mg per hundred cubic centimeters of serum. The bladder contained, respectively, 120 and 480 cc of residual urine on two occasions, and cystoscopic examination revealed a cystic mass, 3 cm in diameter, with the meatus on the posterolateral aspect, apparently not communicating with the mass. There was chronic diffuse cystitis and right pyelonephritis with atrophy and ureteritis. At examination a few days later, the note was made that although fluctuation in the size of the mass was not seen, the possibility of its being a ureterocele was suggested.

Right nephrectomy was advised, at operation the right kidney was found to be atrophic, and on that side there was duplication of the ureters one of which

51 Bumpus, H. C., Jr. Ureteral Scissors, *J. A. M. A.* **83** 1331 (Oct 25) 1924.

52 Romaine, F. W. Report of a Case of Cyst of the Left Ureteral Orifice. *J. Urol.* **11** 489, 1924.

53 Blum, Victor. Die intravesikale blasige Erweiterung und der Prolaps des unteren Harnleiterendes, *Arch. f. klin. Chir.* **113** 131, 1920.

was the site of a huge hydro-ureter. Nephro-ureterectomy seemed advisable, and accordingly both ureters were severed from the bladder and removed with the kidney. The normal sized ureter was joined to the hydro-ureter in an ampulla-like swelling just before it joined the mucous membrane of the bladder, this measured 2.5 cm. in length, and was dilated to about the same width, bulging into the cavity of the bladder. Above and below this, the ureter was constricted.

At cystoscopic examination nineteen days after operation the cystic tumor in the bladder was reduced to about one-third its former size.

CASE 2—A man, aged 25, five years previously had had acute gonorrheal urethritis. He complained of urinary difficulty, which he had had as long as he could remember, and which consisted of burning, frequency and nocturia, strain-



Fig. 1 (case 1)—Right kidney with two ureters, one of which is a hydro-ureter.

ing, dribbling and voiding of an interrupted stream. He had "always" had soreness in the right flank, but no colic, although at times, when voiding, sharp pain radiated from the bladder upward to the region of the right kidney. Following a siege of influenza four months before coming to the clinic, all urinary symptoms had been aggravated, the attacks of pain in the right flank had become severe, and were accompanied by chills and fever.

On general examination the patient appeared ill. Urinalysis revealed red blood cells graded 1 and pus graded 4. The erythrocyte count was normal, and there was no increase in the number of leukocytes. Blood urea was estimated at 20 mg. per hundred cubic centimeters, and roentgenographic examinations of the kidneys, ureters and bladder gave negative results. The cystogram, however,



revealed a normal outline of the bladder with an egg-shaped filling defect on the right side. On cystoscopic examination, a rounded mass was seen "projecting from the right of the trigone, with broad attachment, smooth, soft, but not translucent, the right meatus was not seen." Functional tests of the two kidneys separately showed that the right kidney was functionless. A diagnosis was made of ureterocele or benign tumor of the bladder, with functionless right kidney, and operation was advised.

On the evening of admission to the hospital, the patient had a severe chill, and the temperature mounted to 103 F, where it remained with but little variation



Fig. 2 (case 2) —Right kidney with hydro-ureter

for three days after which it dropped abruptly to normal. During this time, there was intermittent severe pain in the right lower part of the abdomen, radiating up to the region of the kidney, and marked tenderness in the right lower quadrant and flank. The leukocyte count increased from 8,500 to 12,500 cells per cubic millimeter.

After an interval of four days, during which the temperature maintained a normal level, and the leukocyte count returned to normal, suprapubic exploration of the bladder was performed. A huge ureterocele sac was found projecting into the bladder from the region of the right ureteral orifice, the tumor measured approximately 6.5 cm in length and 3.5 cm in diameter. The ureteral orifice was seen at its apex. The ureter was about 2.5 cm in diameter throughout its

upper third, the lower portion was bulbous and measured about 4.5 cm. in diameter. There was hydronephrosis, with destruction of considerable renal substance. The ureterocele was resected, the mucous membrane of the bladder was closed with interrupted sutures of catgut and the ureteral stump was ligated. The ureter was then dissected free from the bladder and freed almost up to the level of the kidney. The suprapubic wound was then closed, with a no. 30 catheter in the bladder and two Penrose eigaret drains in the right perivesical space. The patient was then turned on the left side and the right kidney and ureter were removed intact.

The report of the pathologist included hydronephrosis, with destruction of about 70 per cent of the renal substance, ureterocele and markedly dilated ureter. The patient had an uneventful convalescence and was dismissed from the hospital three weeks after operation in excellent general condition.

#### COMMENT

In neither of these cases was a positive diagnosis made by cystoscopy. Although ureterocele was considered in each, neither presented the usual appearance of ureterocele at cystoscopic examination, the intermittent ballooning and translucency were absent. The etiology is not clear in either case. In one case, the condition was associated with a congenital anomaly of the urinary tract. In both cases, in all probability, the condition had been present for a longer time than the duration of severe symptoms, which in the first case evidently were due to superimposed infection and in the second to obstruction at both ureteral and urethral orifices. Pyuria had been a persistent symptom in both cases. The radical method of treatment was deemed advisable in view of the infected functionless kidneys and the associated pathologic changes in the ureters. In one case the ureterocele sac was resected transvesically, in the other it was not disturbed.

# CHANGES IN THE HEAD OF THE FEMUR AFTER COMPLETE INTRACAPSULAR FRACTURE OF THE NECK

THEIR BEARING ON NONUNION AND TREATMENT

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In a discussion of the changes in the head of the femur following a complete intracapsular fracture of the neck, a preliminary consideration of its blood supply is necessary for a proper comprehension of the secondary changes which may take place in it

It is generally accepted that the main blood supply of the femoral head comes from

1 The ligamentum teres Hyrtl,<sup>1</sup> Senn<sup>2</sup> and Langer<sup>3</sup> considered the vessels running through this ligament of little importance and thought that they became obliterated in old people, but recently Schmorl<sup>4</sup> showed in a study of serial sections that the vessels of the round ligament are active even in old age. He cited a case in which, in spite of fracture of the neck of the femur and complete destruction of the capsule, the whole head was adequately nourished through the vessels of the ligamentum teres. This was also proved by Basset<sup>5</sup> and Frangenheim<sup>6</sup>. Frangenheim found permeable although somewhat thickened vessels present in the ligamentum teres of a person 85 years of age. Nussbaum,<sup>7</sup> likewise, was able to demonstrate anastomosis between the arteries of the ligamentum teres and the network of vessels in the head of the femur in a man 60 years old. Iselin<sup>8</sup> proved experimentally that

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\* Submitted for publication, Sept 10, 1929

<sup>1</sup> From the Department of Surgery, The University of Chicago

<sup>2</sup> This work has been conducted under a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago

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interruption of the blood vessels in the ligamentum teres does not necessarily lead to serious consequences in the femoral head

2 The capsular arteries It is generally agreed that the main vascular supply of the femoral head comes from the branches of the capsular arteries Schmorl<sup>4</sup> and Nussbaum<sup>7</sup> described the main vessels as being at the upper and lateral parts of the capsule Frangenheim<sup>6</sup> thought that these vessels are at the anterosuperior aspect of the capsule Nelidoff<sup>9</sup> found them at the posterior aspect of the capsule Lexer<sup>10</sup> and Waldenstrom<sup>11</sup> thought that the lateral two thirds of the head is supplied by capsular branches running along the upper margin of the femoral neck Another vessel, which supplies only the medial third of the head, is found along the lower margin of the neck These vessels are also the main source of nutrition for the femoral neck

From a survey of these anatomic studies it would seem plausible that in an extracapsular fracture, as in the intertrochanteric or peritrochanteric region, when there is preservation of part or all of the capsular attachment, there is absence of, or only negligible interruption of, nutrition from the capsular vessels On the other hand, a complete medial or intracapsular fracture, especially of the subcapital type, will sever capsular connections and interrupt the main source of blood supply to the head The head in this case, however, may still be nourished by the vessels of the ligamentum teres and by the synovial fluid For the satisfactory study of the changes in the femoral head after such a fracture, it is necessary to utilize cases in which there is a separation of the fragments, and others in which there is impaction or contact between the fracture surfaces Fifteen selected cases have been studied In the first group, two types of cases will be considered, namely, those in which the head fragment is necrotic, and those in which it is alive in part or whole, and its nutrition adequately maintained by the vessels of the round ligament In the second group, I shall consider cases in which bony union has not yet occurred, and those in which bony consolidation eventually resulted

#### SEPARATION OF THE FRAGMENTS

Cases 1, 2, 3 and 4 are cited to show that, following the fracture the head may subsequently undergo total necrosis, which later is followed by secondary disintegrates and reconstructive changes in it

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## CASE 1 (NECROTIC HEAD)

Case 1 indicates the possibility of marked secondary vascularization and organization of the greater part of the marrow and a small amount of the dead bone of the necrotic head from the ligamentum teres

The patient was a woman, aged 54. Two months before examination, she fell on her right hip, following which she received no treatment but had pain and loss of function necessitating the use of crutches in walking. A roentgenogram showed an ununited intracapsular fracture of the neck with considerable erosion of both fragment ends. The head retained its normal density, except in its superior portion and in its inferior portion near the junction with the neck, where the density was slightly reduced. The innominate bone and the distal fragment of the femur showed a slight atrophy from disuse (fig 1).



Fig 1 (case 1)—Roentgenogram of the hip, two months after the injury, showing normal density of the greater portion of the femoral head and atrophy of disuse of the innominate bone and distal fragment of the femur

A Whitman reconstruction operation was performed. The joint cavity was found to be filled with a serohemorrhagic fluid. The neck of the femur showed an intracapsular fracture with complete detachment of the fragments. Most of the neck on either fragment had been eroded away. The sharp edge of the lower part of the distal fragment of the neck fitted into a deep cavity which had been eroded in the under surface of the proximal fragment. In removal of the head the ligamentum teres tore near the acetabulum, and a spurting artery was seen in the stump, indicating an increased blood supply entering by this route.

*Macroscopic Appearance of the Excised Head*—The articular surface of the head of the femur showed a fairly regular hemispherical contour (fig 2A). The surface was covered by bluish-white, glistening articular cartilage. The round ligament was enlarged and hyperemic. Around the fovea there had been

a small amount of absorption of cartilage and replacement by connective tissue. The fracture surface showed erosion of the neck up to the margins of the articular cartilage, except for a protrusion of dense bone 1 cm long at its central portion. Beneath this was a cup-shaped erosion, 1 cm deep, which was produced by the protruding portion of the lower part of the neck. Its surface was hard as a result of the eroded bone dust that had been ground into the cancellous spaces.

A coronal section was made of the head passing through the fovea (fig 2*B*). The bone was found to be of normal density and the articular cartilage of normal thickness. The bone was yellowish white in its peripheral portion. But invading the head from the fovea was a dark gray band of tissue extending across the fragment almost to the fracture surface. It appeared to be young connective tissue and blood vessels that had grown in from the round ligament.

*Microscopic Appearance*—The articular cartilage was of normal thickness and was attached to the underlying bony cortex, but it was necrotic in its entire

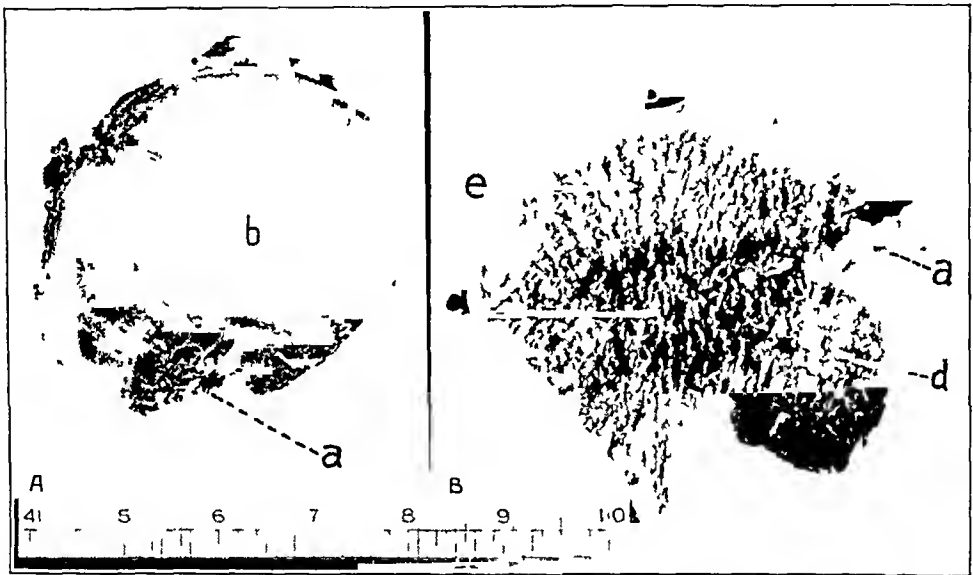


Fig 2 (case 1) —*A*, appearance of half of the removed femoral head, showing attachment of the ligamentum teres (*a*) and normal contour of the head with slight erosion of the cartilage about the fovea (*b*). *B*, freshly cut section of the head showing a portion of markedly hypertrophied ligamentum teres (*a*), intact articular cartilage (*b*), invading connective tissue (*c*), pinkish spongiosa with fresh bleeding (*d*) and normal bony trabeculae (*e*).

extent (fig 3). Most of the cartilage cells had broken down, a few showed shrunken, fragmented, poorly stained nuclei. The superficial layer of cartilage immediately surrounding the fovea was eroded and replaced by connective tissue apparently extending from the round ligament, which showed marked hypertrophy and increased vascularity. The deeper layer of the cartilage showed slight calcification. All of the old bone and bone-marrow of the head were necrotic. That in the yellowish peripheral portion, which comprised approximately one third of the specimen, remained uninvaded, and its trabeculae were of normal size. In the dark central zone, the necrotic marrow had been absorbed and replaced by vascular young connective tissue, fat and fibroblasts. A very small amount of new bone

was being laid down in the connective tissue and on the old necrotic trabeculae, and in places the old bone was being absorbed (fig 4). These bone lamellae lay in a matrix of loose fibrous connective tissue containing many dilated blood vessels and densely infiltrated with red blood cells, osteoblasts and hemopoietic cells. This highly vascularized tissue replacing the dead marrow formed a more or less diffused zone which extended from the ligamentum teres to the fracture surface below in the region of the eroded pit and peripherally to near the junction of bone and cartilage at the rim of the femoral head. The deep crypt on the fracture surface was lined by small fragments of dead bone that had been ground into the cancellous spaces by pressure from the opposing bone. In places, these fragments were surrounded by vascular connective tissue, and showed new bone formation and lacunar absorption.

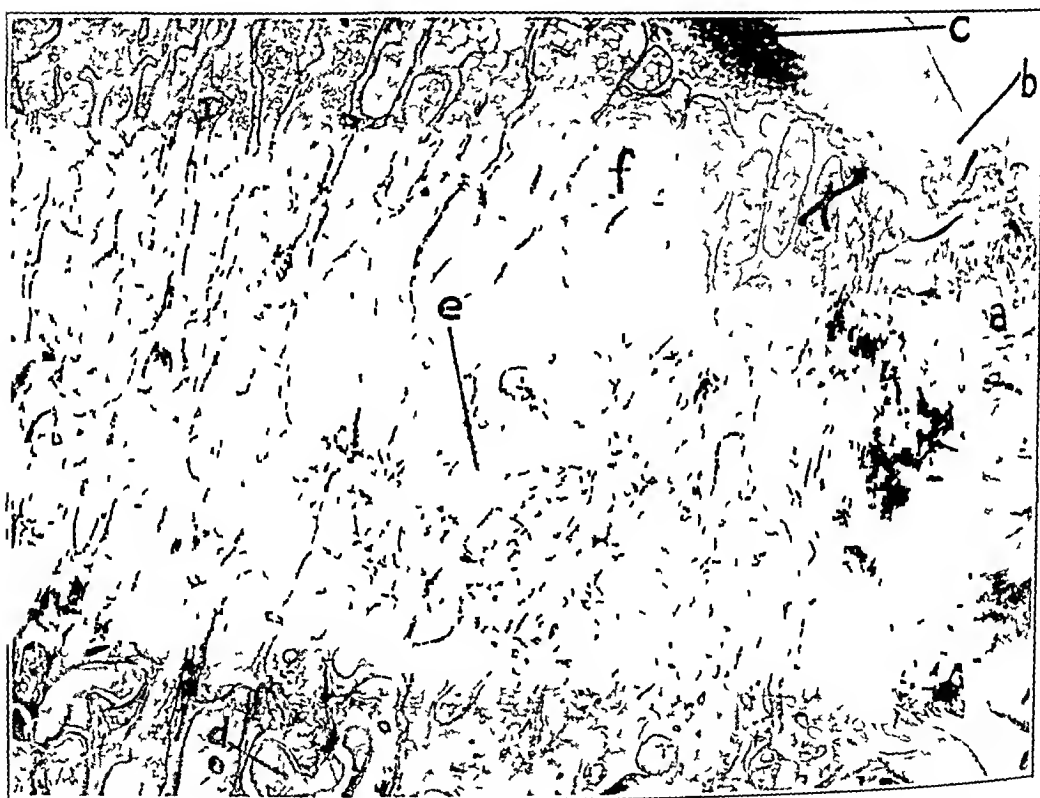


Fig 3 (case 1) —Area of attachment of the ligamentum teres. Note ligamentum teres with numerous blood vessels (a), fibrous tissue invasion of the cartilage (b), slightly calcified cartilage (c), numerous dilated blood vessels in the marrow (d), highly vascularized fibrous marrow (e) and degenerated and unreplaced marrow with necrotic bony trabeculae (f). Reduced from a magnification of  $\times 60$ .

*Summary*—Summarizing the case, one has

- 1 Nonunion of an intracapsular fracture of the neck of the femur of two months' duration with apposition of the fragments
- 2 Very little decrease in the density of the head but atrophy of disuse of the distal fragment and pelvis
- 3 Necrosis of the entire head, including bone, cartilage and bone-marrow
- 4 Invasion of about two thirds of the cancellous space of the necrotic head by vascular connective tissue extending from the fovea across the central portion to the

fracture surface, very slight bony transformation going on in this region as a result of absorption of the old necrotic bone and replacement of it by newly formed bone

5 Marked hypertrophy and vascularization of the ligamentum teres

6 Slight erosion of the articular cartilage with fibrous tissue replacement about the fovea

#### CASE 2 (NECROTIC HEAD)

Case 2 also showed secondary invasion of the necrotic head by vascular connective tissue from the region of the ligamentum teres with subsequent absorption of the necrotic lamellae and formation of a small amount of new bone in this region. Marked erosion of the

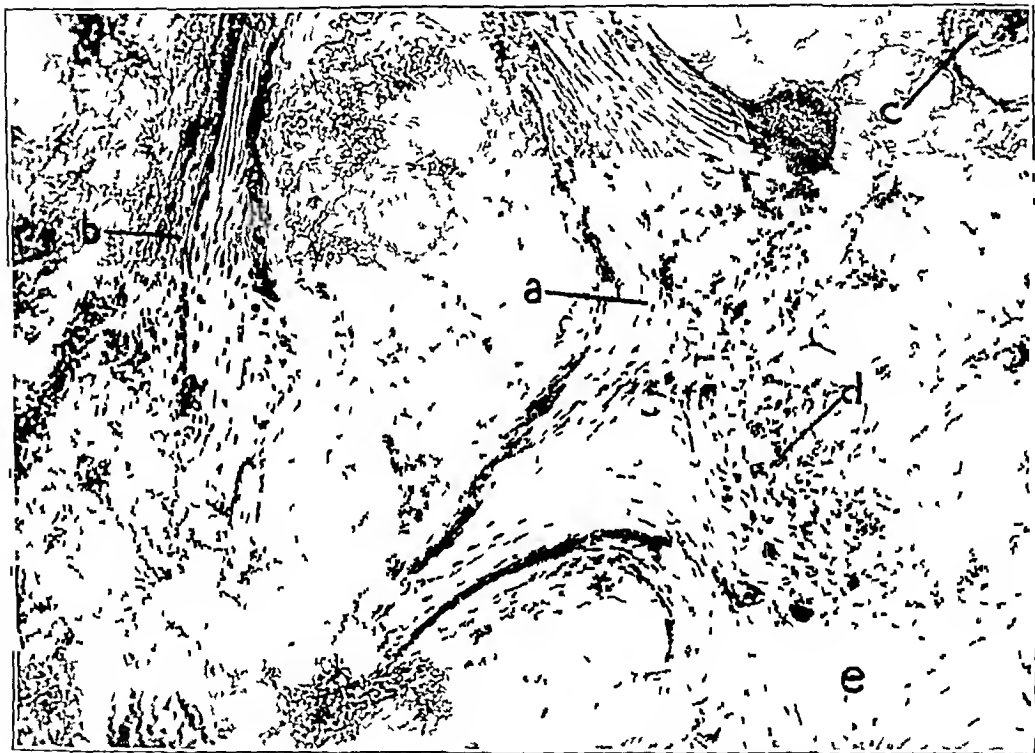


Fig 4 (case 1)—Area of regenerative and absorptive processes. Note newly formed bone (*a*), osteoblast (*b*), dilated blood vessels (*c*), multinucleated giant cell (*d*) and necrotic bony trabeculae (*e*). Reduced from a magnification of  $\times 160$ .

articular cartilage and underlying spongiosa about the fovea occurred in this head.

The patient was a woman, aged 57. Sixteen months before examination, she fell on her right hip, and thereafter suffered marked pain and disability in it. A roentgenogram at that time showed an intracapsular fracture of the neck of the right femur. A closed reduction was performed on the same day, and the body and extremity were placed in a long plaster spica, which remained on for eight weeks. The cast was then removed, but on account of the persistent disability and pain in the right hip, she remained in bed for five months. After that, she walked on crutches. The roentgenogram showed nonunion, with complete erosion of the



neck fragments. The head cast a shadow of normal density, except for a narrow margin about the fovea, where it was reduced (fig 5). The distal fragment and innominate bone showed atrophy of disuse.

A Whitman reconstruction operation was performed. The fragments were found separated with the head lying in the acetabulum and the end of the distal fragment displaced upward. The ligamentum teres was small, and no spurting artery was seen when the head was removed. The neck portion had been completely eroded, and the fracture surface was largely covered by an overgrowth of connective tissue from the capsule.

*Macroscopic Appearance of the Excised Head*—The fovea was occupied by a narrow ligamentum teres, which readily tore out from its attachment to the head. The head showed an almost normal contour, except for an area 2 cm in diameter about the enlarged fovea, where a depression was encountered (fig 6A). In this region, the articular cartilage and the subchondral bone were eroded, exposing a

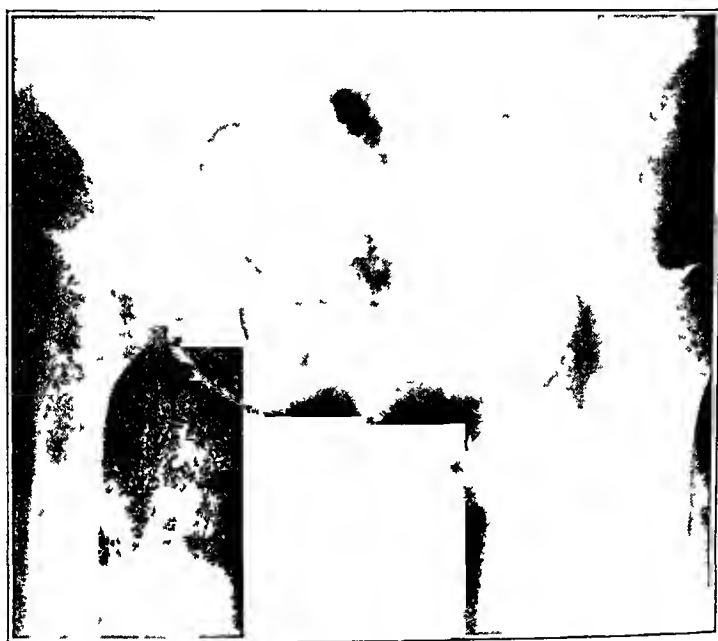


Fig 5 (case 2) —Roentgenogram of the hips. Note the marked absorption of the neck of the right femur. The head cast a dense shadow, except for a small invaded area at the fovea, which showed reduction in density.

dark-staining spongiosa. The rest of the articular surface of the head was covered by whitish, glistening cartilage. The fracture surface was lined by small fragments of bone to which a small amount of fibrous tissue was adherent.

The femoral head cut with normal resistance. The cut surface showed the defect at the superior portion of the head (fig 6B). This was lined by a darkly stained tissue, which extended down into the underlying spongiosa. The rest of the spongiosa was yellowish. The articular cartilage was intact, except at the margin of the erosion about the fovea, where it was lifted and undermined by the darkly stained spongiosa.

*Microscopic Appearance*—The articular cartilage was necrotic and showed marked calcification in the deeper layer (fig 7). Most of the cartilage spaces were empty, while a few were occupied by small, shrunken, poorly staining cells. At the margin of the erosion about the fovea, the cartilage was lifted and undermined by an ingrowth of vascularized connective tissue. Lining this erosion and

extending down deep into the spongiosa was a rather loose, cellular, vascularized connective tissue. Embedded in this, especially along the floor of the erosion, were necrotic bony trabeculae which showed simultaneous absorption and formation of new bone. Red blood cells, monocytes and osteoblasts were also seen about the necrotic lamellae. Immature fibroblasts pushed their way from the invading vascularized connective tissue into the surrounding necrotic fatty marrow. This gradually merged into a clear area away from the fovea and along the fracture surface, where the necrotic bony lamellae showed no signs of absorption or regeneration. They were surrounded by a dead marrow made up largely of fat spaces.

*Summary*—The case may be summarized as follows

1 Intracapsular fracture of the neck of the femur with wide separation of the fragments

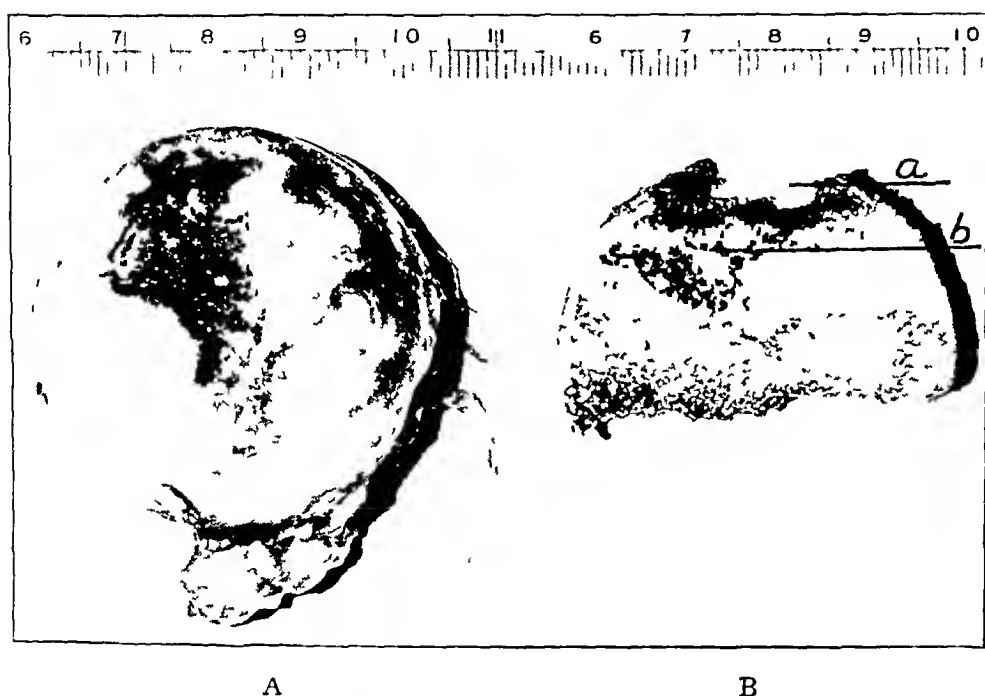


Fig 6 (case 2) —A, appearance of the femoral head showing the erosion about the fovea. B, freshly cut surface of the femoral head showing erosion (a) and invaded and vascularized portion (b).

2 Normal density of the head, except for slight rarefaction in its superior half, marked absorption of the neck. Atrophy of disuse of the distal fragment and of the innominate bone

3 Necrotic femoral head

4 Presence of a ligamentum teres

5 Invasion of the necrotic head by vascularized connective tissue from the fovea downward into the upper half of the fragment

6 Marked absorption of the articular cartilage about the fovea

7 Formation of a very small amount of new bone and bone-marrow and absorption of old necrotic bone in the secondarily vascularized region

## CASE 3 (NECROTIC HEAD)

Case 3 is cited to indicate that the superior portion of the necrotic head pressing against the acetabulum may be traumatized and the cartilage and bone thereby undergo extensive destruction. Secondary invasion of the necrotic head from the ligamentum teres and surrounding capsule may occur with simultaneous absorption of dead bone and formation of new bone.

The patient was a woman, aged 44. Thirteen months before examination, she fell on her right hip and subsequently suffered pain and limitation of motion at



Fig 7 (case 2) —Microscopic section of the invaded portion of the head. Note necrotic articular cartilage (*a*), markedly vascular and fibrous marrow (*b*) and new formed bone on a necrotic trabecula (*c*). Reduced from a magnification of  $\times 160$ .

the hip. The roentgenogram taken of the hip at the time showed an intra-capsular fracture of the neck with separation of the fragments. A closed reduction was attempted, and a long plaster of paris spica applied. This remained in place for ten weeks. Walking thereafter, although possible, produced pain in the right hip. Roentgen examination at this time showed nonunion with a separation of the fragments and marked absorption of the neck (fig 8). The head cast a dense shadow which was uniform except in its lower portion where it is reduced. The neck showed marked rarefaction and absorption. This was verified when

the day after the examination a Whitman reconstruction was performed. At the operation, the head was found embedded in fibrous tissue adhesions in which the ligamentum teres could hardly be identified. It was considerably damaged in prying it out of the acetabulum and a portion was detached bordering on the fovea.

*Macroscopic Appearance of the Excised Head*—The articular cartilage showed marked irregularity with destruction at the superior surface, where there was a defect from injury inflicted during removal and from absorption at the point of attachment of round ligament about 2 cm in diameter (fig 9). The underlying spongiosa in the superior portion was exposed, irregular and fragmented. On the outer circumference of the head there was more of the cartilage that could be seen. Only a narrow strip of fibrous tissue, the remains of the round ligament, was found attached at the fovea. The fracture surface was free from adhesion. It was lined by hard, bony trabeculae, which stood out prominently.



Fig 8 (case 3) —Roentgenogram of the hip showing almost no reduction of density of the femoral head, but marked atrophy of disuse of the distal fragment and the pelvis.

On sawing, the head cut with normal resistance. The cut surface showed a large triangular area devoid of cartilage and subchondral bone in the region of the attachment of the ligamentum teres (fig 10). Extensive and more marked gross destruction and disorganization of the cartilage and underlying spongiosa were seen at one of the osteochondral junctions. In the spongiosa, columns of grayish, soft tissue ran from the articular surface toward the fracture line.

*Microscopic Appearance*—The entire remaining articular cartilage was necrotic and was much thinned at its margins and along the anterior surface. The remnants of the cartilage showed empty cartilage spaces and marked calcification in the deeper layer. While this remaining cartilage was intact along one region of the osteochondral junction, it was detached and fragmented in another with invasion by fibrous tissue. The triangular defect at the superior surface showed also a disappearance of a part of the underlying spongiosa. The sides and apex of this defect were made up of necrotic fragments of bony lamellae lying in a matrix of

dense, practically acellular and avascular fibrous connective tissue similar to that which made up the soft, grayish columns extending from the articular surface to the fracture surface of the head. Signs of absorption of bone and formation of new bone were nowhere to be seen in this region. The detachment, marked destruc-

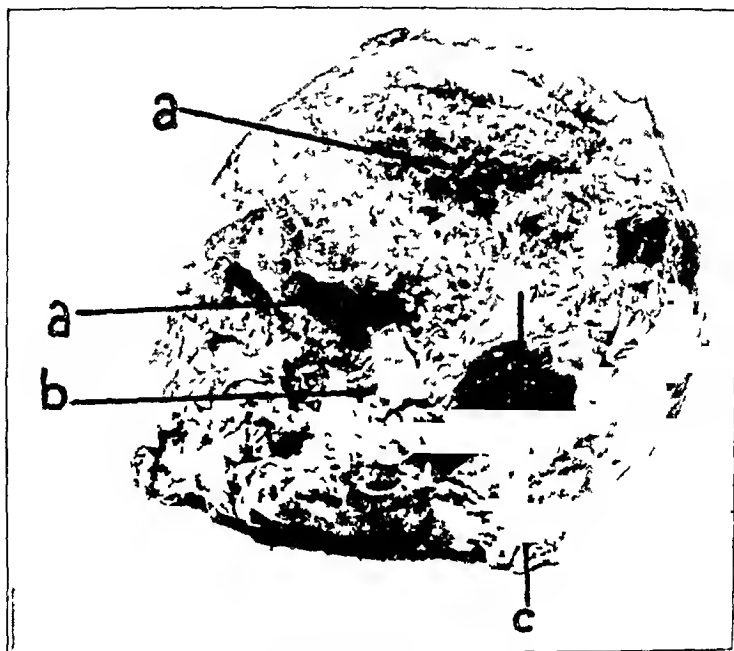


Fig 9 (case 3)—Appearance of the removed femoral head. Note areas of erosion (a), remains of the round ligament (b) and fibrous tissue (c).



Fig 10 (case 3)—Photomicrograph of a section showing defect from erosion and from injury during removal (a), region of marked destruction of cartilage and bone (b), necrotic but intact cartilage and underlying bone (c) and column of invading fibrous tissue in the spongiosa (d).

tion and fragmentation of the articular cartilage and the underlying bony lamellae in one portion of the specimen gave a picture of marked traumatic erosion. Highly vascular connective tissue invaded this area, throughout which hemopoietic and

fatty marrow a small amount of new bone and active absorption of old and necrotic bony lamellae were encountered (fig 11). At about the osteochondral junction, invasion of the calcified layer of the cartilage by the underlying fibrous marrow with formation of new bone was taking place. In between the columns of dense, scarlike connective tissue, the marrow was degenerated and contained numerous large, empty spaces. In the deeper levels, one encountered scattered areas of calcification.

*Summary*—Summarizing the case, one has

1 Intracapsular fracture of the femoral neck with separation of the fragments

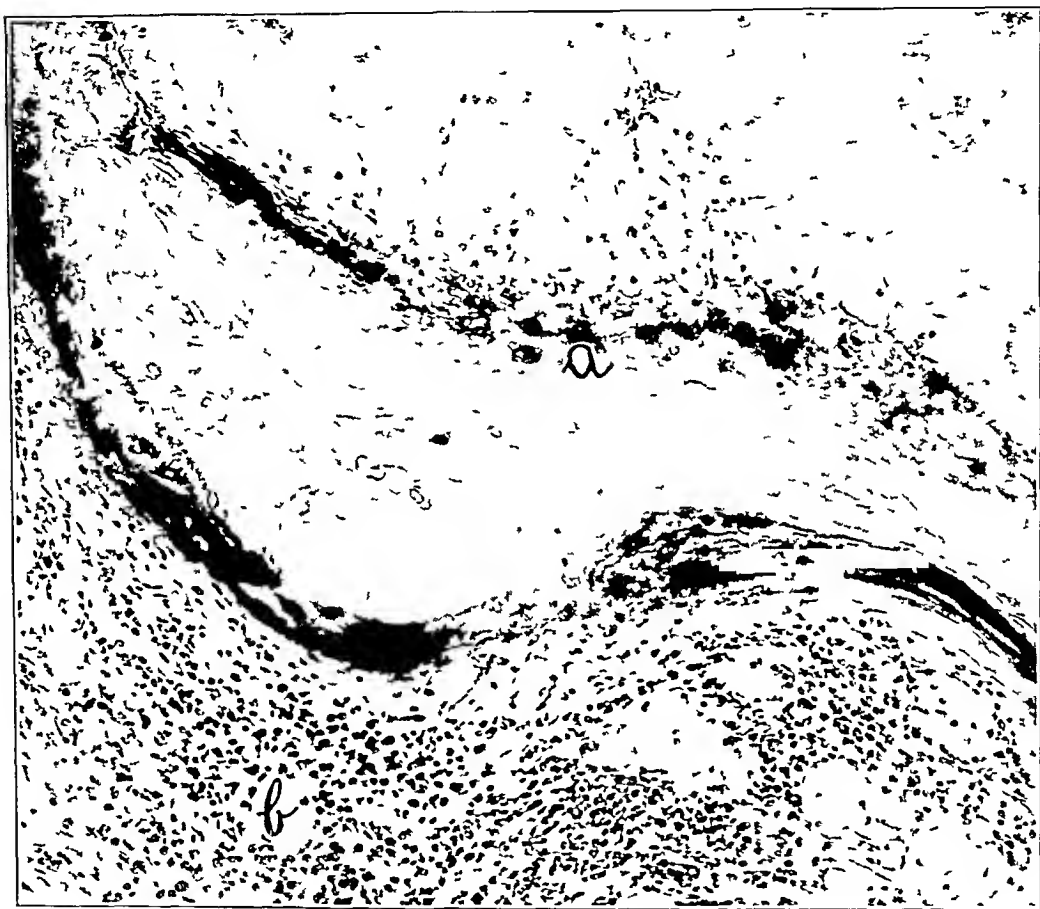


Fig 11 (case 3) —Section of a necrotic bony trabecula showing newly formed bone about it (a) and vascular and cellular marrow (b). Reduced from a magnification of  $\times 160$ .

2 Roentgenogram disclosing dense head with atrophy of the innominate bone and distal fragment of the femur

3 Marked absorption of the neck

4 Totally necrotic femoral head

5 Invasion from the round ligament of about one-half of the necrotic head by vascularized connective tissue which remained fibrous in its peripheral portions and differentiated into bone marrow in its older central portions. Fragments of the cartilage and bone in the upper or traumatized portion of the femur

6 Active absorption of necrotic bone and formation of a small amount of new bone in the region invaded by young vascularized connective tissue

7 Areas of calcification near the fracture surface

#### CASE 4 (NECROTIC HEAD)

Case 4 is cited to show that although the ligamentum teres is present the head may undergo necrosis after its separation from the distal fragment and may fail to be secondarily vascularized by it. In such instances, when the neck is necrotic and eroded, nonunion in spite of good apposition of the fragments may occur. Secondary degenerative changes appear in the head.



Fig. 12 (case 4)—Roentgenogram of the hip, showing nonunion of the fracture a year after closed reduction of the fragments. Note the marked absorption of the neck and the dense head with a small area of rarefaction at the fovea.

The patient, a woman, aged 48, one year before examination fell on her right hip and subsequently began to have pain and marked limitation of motion at the hip. Two days after the accident, she started to walk again but with pain in the hip. The roentgenogram taken two weeks later showed a complete intracapsular fracture of the neck of the femur with separation of the fragments. With the patient under ether anesthesia, a closed reduction was attempted. Four months of immobilization in a plaster of paris spica followed. The cast was then removed, and the patient was allowed to walk with crutches. She still complained of slight pain in the right hip. Roentgen examination showed that the fragment-

were in a fairly good position, but nevertheless nonunion had resulted (fig 12). The head cast an almost normal shadow as contrasted with the marked diffuse decrease in density and marked absorption of the neck of the femur. A Whitman reconstruction operation was performed. At operation, the fragments were found in good apposition, and in removal of the head a narrow ligamentum teres had to be cut.

*Macroscopic Appearance of the Excised Head*—The head had a fairly normal spherical contour, except for slight flattening at the superior surface about the fovea (fig 13A). This region was marked by a loss of cartilage and underlying spongiosa, causing an erosion about 1 cm in diameter. The articular cartilage was clear, whitish and glistening and was slightly undermined about the erosion. The ligamentum teres was made up of a narrow strip of fibrous tissue which easily tore out from its attachment to the head. Areas containing hard spicules of bone were found along the irregular fracture surface. The neck portion of the distal fragment was slightly absorbed, and the interior was occupied by dark, soft, granular marrow containing numerous small pieces of bone.

The femoral head cut with normal resistance. The articular cartilage was intact, except at the region of the fovea, where it was eroded (fig 13B). The

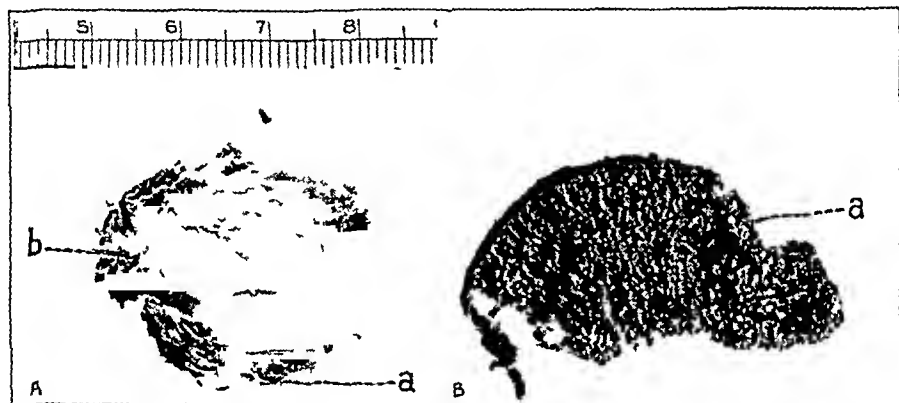


Fig 13 (case 4)—A, photograph of half of the femoral head. Note remains of the ligamentum teres (a) and an area of erosion in the articular cartilage and the underlying spongiosa (b). B, cut surface of the femoral head, showing the area of erosion (a).

remaining cartilage was adherent to the subchondral bone and varied in thickness from 1 to 3.5 mm. The spongiosa had a uniform yellowish, granular appearance.

*Microscopic Appearance*—The head was necrotic. In the region of the fovea, an area of the cartilage, 1 cm in diameter, was eroded, exposing the underlying bony lamellae, which were necrotic and fragmented. A narrow band of fairly vascular connective tissue, presumably extending from the fovea, was seen along the joint surface of the articular cartilage (fig 14). This band, however, had not invaded the spongiosa. Although the remaining cartilage was adherent to the subchondral bone it was necrotic, showed absence of cells and was thin immediately about the erosion. This thinning was due to erosion of the superficial layer by pannus-like connective tissue from the fovea, and to absorption of the deep calcified layer as a result of invasion by the subchondral marrow. This latter process undermined the cartilage in places and lifted it up from the underlying subchondral bone. The bony lamellae everywhere were necrotic, and lay in a matrix of degenerated marrow containing red blood cells and numerous



empty spaces. No signs of absorption of the necrotic bone or formation of new bone could be seen in the spongiosa.

Also of interest were the changes in the neck portion of the distal fragment. They presented a picture of necrosis and absorption. The cancellous spaces were markedly dilated. This dilatation was especially marked about the fracture surface, where the spaces contained a decided increase in fat with a comparatively small amount of lymphoid and fibrous tissue. Embedded in this marrow were small thin-walled blood vessels which had few red blood cells in the lumen. The bony lamellae in this region were necrotic and markedly diminished in size and number. Along the fracture surface, these were reduced to such a degree that only occasional pieces of bone were encountered. An active absorptive process was going on along the periphery of the neck bordering the fracture surface. Here one

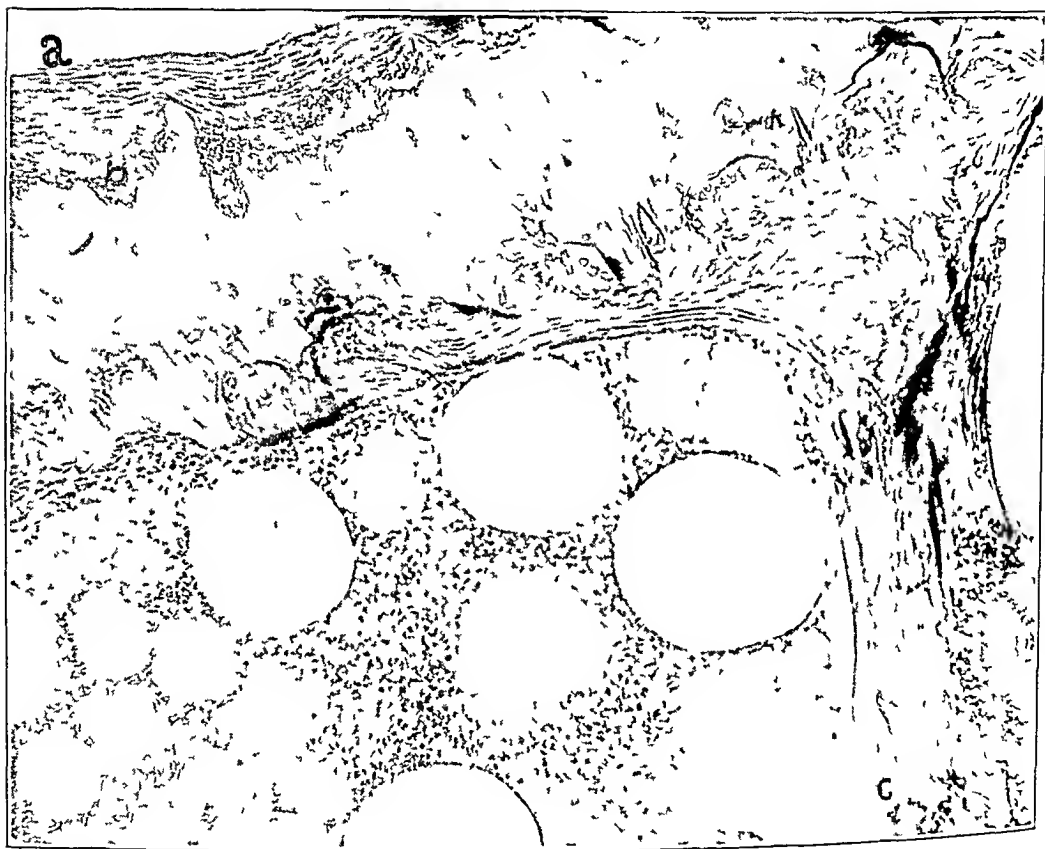


Fig 14 (case 4) —Section of the articular surface showing vascular connective tissue extending from the fovea (*a*), cartilage erosion (*b*) and necrotic bony trabecula (*c*). Reduced from a magnification of  $\times 80$ .

encountered spaces filled by young vascularized connective tissue infiltrated with numerous multinucleated giant cells, red blood cells and a few monocytes. Where these were present there was active and extensive lacunar absorption of the bone. No formation of new bone was seen along the fracture surface. Further down the neck, this merged into a region that presented a picture of partial necrosis. Well staining bone cells still persisted around the haversian canals, although the compact portion of the bone or the region of the intermediate lamellae was marked by their absence leaving dilated and empty lacunae.

*Summary*—The case may be summarized as follows:

1. Early reposition of the fragments, which nevertheless resulted in nonunion.

2 Normal density of the head as shown by the roentgenogram with erosion of the neck

3 Totally necrotic femoral head with failure of vascularization from the ligamentum teres

4 Erosion of the articular cartilage about the fovea with destruction and fragmentation of the underlying bony lamellae

5 Failure of absorption of bone, and of formation of new bone in the spongiosa

6 Erosion and necrosis of the neck portion of the distal fragment

#### COMMENT ON CASES OF NONUNION IN WHICH HEAD BECAME NECROTIC

As may be noted from the descriptions of the specimens, all the femoral heads became necrotic after the fracture. The ligamentum teres was found intact in every instance and showed varying degrees of development. Except in case 4, proliferating connective tissue proceeding from the region of the fovea was seen invading the articular cartilage and spongiosa of the head. These changes show that although the round ligament is present, a separated femoral head, owing to insufficient nourishment, may undergo necrosis after complete intra-capsular fracture of the neck of the femur, and that secondary vascularization of the head from it may or may not occur. On the other hand, the round ligament may be well developed and its vessels may penetrate even the deeper layers of the spongiosa, as in cases 1 and 2, or young proliferating connective tissue may gain entrance either through the fovea (Bonn) or through adhesions along the surface of the eroded neck or articular cartilage, as in case 3, and invade the spongiosa. Consequently, varying degrees of secondary vascularization and organization of the head occur. In cases in which this vascularization is marked and extensive, an organization or replacement of the necrotic head and efficient nourishment of the greater part of the head allowing active formation of new bone may result. This is well illustrated by cases 1 and 2, in which a transformation and partial organization of two thirds and one half of the heads, respectively, occurred after the injury. The activity of such revascularization varies greatly in different cases. In case 1, a transformation of the necrotic marrow and to a very slight extent of the necrotic bone of nearly two thirds of the head occurred within a period of two months, in case 2 similar organization of one half of the head had resulted by the end of sixteen months. Hess previously showed that the ligamentum teres frequently contains large arteries that penetrate into the spongiosa of the head until late in life. These vessels may so proliferate as not only to organize and preserve considerable parts of the femoral head but also to permit an active regeneration of bone. The bone apparently forms by metaplasia of the invading fibroblasts or angioblasts as advocated by Petrow and Baschkirzew for the replacement of the necrotic bone in a transplant. However some of it may come from osteoblasts surviving about the fovea.

Necrosis of the femoral head following complete intracapsular fracture of the neck of the femur has been known since the time of Sir Astley Cooper, nearly one hundred years ago. In 1896, Kocher<sup>12</sup> and more recently Axhausen<sup>13</sup> and Bonn<sup>14</sup> expressed the opinion that every subcapital fracture of the neck results in necrosis of the head.

The possibility of secondary vascularization of a necrotic head was less well known until the recent studies of several investigators, prominent among whom were Schmorl,<sup>4</sup> Hesse<sup>15</sup> and Bonn<sup>14</sup>. It was from the work of these observers that secondary vascularization of the necrotic head became recognized. The first two authors believed that the ligamentum teres itself proliferates and causes the revascularization of the head. They observed it to be so well developed even in advanced age that not only a revascularization and replacement of considerable portion of the necrotic head but also an active regeneration of bone and some callus formation often occurs. Bonn, however, after studying several preparations of femoral heads following intracapsular fracture of the neck of the femur, stated that the ligamentum teres is important for the nutrition or revascularization of the head only in that it serves as the portal of entry for proliferating connective tissue to penetrate and invade the spongiosa and replace the necrotic head.

Necrosis of the head, partial or complete, predisposes to secondary transformative changes in it. This is a common occurrence in necrotic structures as in free bone and cartilage transplants, which appear to have markedly reduced resistance to any kind of injury and invasion by fibrous connective tissue. If the necrotic head fails to be secondarily vascularized from the ligamentum teres, simple destruction and fragmentation of the articular cartilage and the underlying bony lamellae occur in the traumatized region. This structural disorganization is seen more in the region that received the greatest amount of injury. If an active invasion of the head by a pannus-like connective tissue extending from the ligamentum teres occurs, there is apt to be an early erosion with replacement of the cartilage and bone about the fovea. This erosion serves subsequently as the portal of entry into the spongiosa for proliferating connective tissue. The deep layer of the remaining articular cartilage is then attacked and gradually absorbed from the interior by the subchondral fibrous marrow with or without formation

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12 Kocher, T. Beiträge zur Kenntnis einiger praktisch wichtiger Frakturformen, Basel und Leipzig, *Formen Hfts* 10, 11 and 12, 3 R., of Mitt a Klin u med Inst d Schweiz, 1895-1896, p 585.

13 Axhausen, G. Die Nekrose des proximalen Bruchstucks beim Schenkelhalsbruch und ihre Bedeutung für das Hüftgelenk, *Arch f klin Chir* **120** 325, 1922.

14 Bonn, R. Zur Frage der knöchernen Heilung subkapitaler Schenkelhalsfrakturen, *Arch f klin Chir* **134** 270, 1925.

15 Hesse, F. Zur pathologischen Anatomie der Schenkelhalsfrakturen, *Arch f klin Chir* **134** 141, 1925.

of new bone in the cartilage layer. Even an actively revascularized and considerably organized necrotic head undergoes secondary degenerative changes following traumatism, as from rubbing together of fragment ends and invasion by proliferating connective tissue.

In case of nonunion the head has relatively little stress thrown upon it as it participates but little in weight-bearing. However, there may be enough pressure against it from the distal fragment to erode the neck and to break down bony trabeculae and necrotic cartilage at the point of greatest pressure against acetabulum. The very slow rate of absorption of necrotic portions and replacement by new bone results from this disuse. Hence the dead head may cast a heavier shadow than the surrounding bone for two or three years before it is transformed. Functional stimulation is essential for rapid revascularization, absorption and transformation when the conditions for the invasion of blood vessels are favorable. Its influence will be shown later in cases reported in which bony union occurred in the presence of a necrotic head and transformation took place more rapidly.

#### CASE 5 (LIVE HEAD)

A femoral head, however, which becomes completely separated after an intracapsular fracture of the neck of the femur may, instead of becoming necrotic, be preserved and kept alive by an adequate nourishment from the vessels of the ligamentum teres. Case 5 is cited to indicate that the separated head may remain alive and be adequately nourished by the vessels of the ligamentum teres and, when the fracture is recent, it may show only slight atrophy subsequent to the loss of function. Gross destruction of the cartilage and bone generally fails to occur, although beginning invasion and replacement of the deeper layer of the articular cartilage at its superior portion by the subchondral fatty marrow may be encountered.

The patient was a man aged 60. Sixteen months before the examination, he was struck on the right thigh by the fender of an automobile. He had pain and loss of function of the hip and remained in bed for thirty-three days at which time a roentgenogram was taken which was reported to show nonunion of a fracture of the neck of the femur. Reduction with the patient under ether anesthesia was performed, and the leg was kept immobilized with weight extension for ten weeks. He was then allowed to be up and about on crutches. Another roentgenogram was taken on the day of admission, and this showed nonunion and erosion of neck fragments. The head revealed a slight diffuse decrease in density (fig 15). A Whitman reconstruction operation was performed. At operation, the ligamentum teres was found intact. There was a cavity between the fragment ends and adhesions between the margins of the head fragment and the surrounding capsule.

*Macroscopic Appearance of the Excised Head*—The head showed a normal spherical contour (fig 16). The articular cartilage was intact and showed no loss of substance. It was smooth, clear, yellowish and glistening. A small ligamentum teres was found attached at the pole. The fracture surface was irregular and covered by a fibrous layer beneath which was a newly formed layer of bone.

The head cut with decreased resistance. The cut surface revealed an intact articular cartilage which varied from 3 to 5 mm in thickness. The spongiosa was increased in amount and had a uniform yellowish, trabeculated appearance.

*Microscopic Appearance*—From a general survey of the head it was found to be alive. The articular cartilage was normal, except for slight calcification.



Fig 15 (case 5)—Roentgenogram showing a diffuse decrease in density of the head of the right femur



Fig 16 (case 5)—Appearance of the femoral head showing normal contour and intact articular cartilage

of the deep layer and the presence of a thin layer of perichondral fibrous tissue along its joint surface about the fovea. The cartilage cells were present and stained well. At the superior surface about the region of the fovea the articular

cartilage was invaded from the interior by the subchondral fatty marrow, forming marrow cavities and vascular spaces in the cartilage (fig 17). With the encroachment of the subchondral marrow, there was a simultaneous replacement and thinning of the articular cartilage in this region. These chondral marrow cavities contained fat cells, blood vessels, red blood cells, few monocytes and multinucleated giant cells. Strips of newly formed lamellar bone could be found partially lining these cavities. Although the bony trabeculae showed considerable diminution in number and size, they still retained normal-appearing bone cells (fig 18). These lamellae lay in a matrix of markedly fatty marrow containing a few blood vessels, red blood cells and monocytes. Only in a small region at the fracture surface did this fatty marrow merge into a limited zone of slightly vascular connective tissue. Embedded in this tissue was a small amount of newly formed

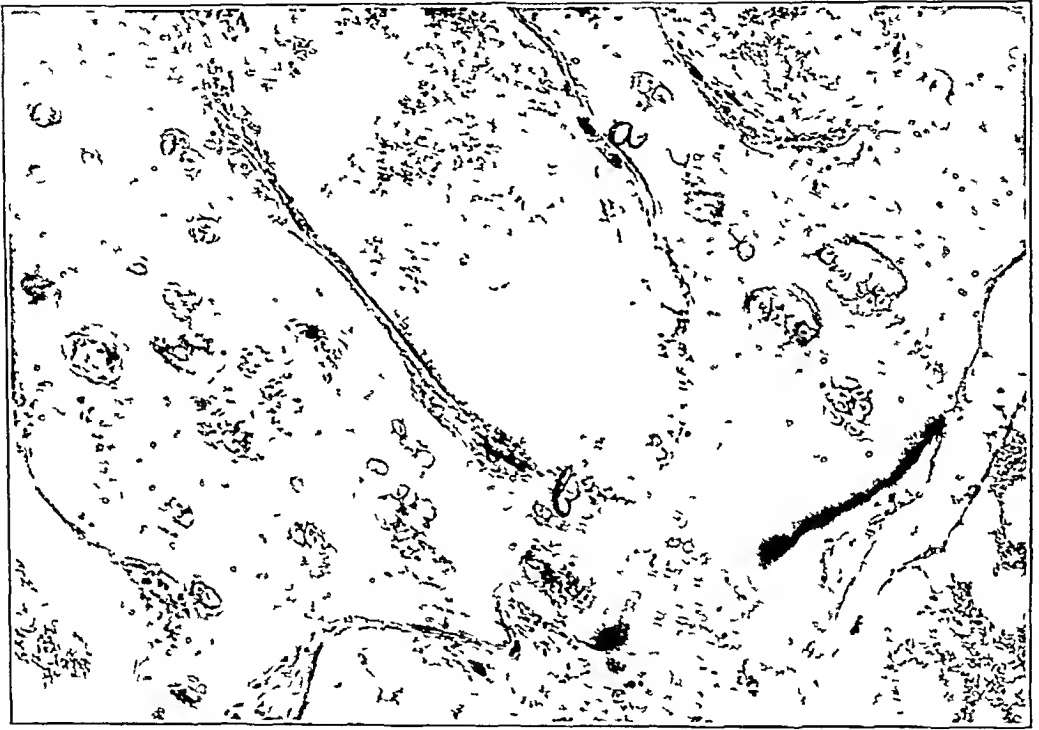


Fig 17 (case 5) —Invasion of cartilage by the subchondral fatty marrow and vascular spaces, showing multinucleated giant cells (a) and newly formed lamellar bone (b). Reduced from a magnification of  $\times 80$ .

bone surrounded by many osteoblasts. Despite the presence of this vascularized connective tissue, no evidence of absorption of bone was seen in the proximal fragment. A synovial covering was present over a portion of the fracture surface bordering on the cavity.

*Summary*—The case may be summarized as follows:

- 1 Nonunion of fracture of the neck with erosion of the fragments of sixteen months duration. Diffuse decrease in density of the head.
- 2 Living although atrophied head fragment with slight formation of new bone at one end of the fracture surface.
- 3 Intact ligamentum teres.

4 Invasion and replacement of the slightly calcified deeper layer of the superior portion of the articular cartilage by the subchondral marrow, with formation of narrow strips of new lamellar bone about the marrow cavities thus formed

#### CASE 6 (LIVE HEAD)

Case 6 indicates the marked atrophic change that a separated but live head of the femur may undergo after four years. A marked replacement and thinning of the superior portion of the articular cartilage due to invasion by the subchondral marrow are noted.

The patient, a woman, aged 58, four years before examination fell on her left hip. Subsequently, the hip became so painful that weight bearing and movement



Fig 18 (case 5) —Section of the spongiosa showing living bone trabecula (*a*), dilated fatty marrow cavity (*b*) and blood vessels (*c*). Reduced from a magnification of  $\times 160$ .

were impossible. A closed reduction with the patient under ether anesthesia was performed four days after the injury. Nine months of immobilization in a plaster of paris cast followed, without improvement. Treatment was finally discarded, and from then until the time of the operation the patient used crutches. A roentgenogram of the hip at the time of examination showed an old intracapsular fracture of the neck of the femur with complete erosion of the fragments of the neck (fig 19). The head revealed considerable diffuse decrease in density. A Whitman reconstruction operation was performed, and the head with an intact ligamentum teres was found in the acetabular cavity. The neck was completely eroded and the end of each fragment was bordered by a thin cortex of new bone which was covered by a thin fibrous layer from which sprang adhesions running to the capsule at its upper limit.

*Macroscopic Appearance of the Excised Head*—The articular cartilage appeared whitish, clear and shiny without any irregularity, except at the fovea, where a small tag of fibrous tissue, presumably a part of the round ligament, was found attached (fig 20). There was a slight thinning of the superior surface of the cartilage over an area 2 cm in diameter. The underlying spongiosa was distinctly visible through this thin, bluish articular cartilage.

The specimen cut easily and was abnormally soft, except at the eroded neck surface, where it had normal bony resistance (fig 21). The cut surface revealed an articular cartilage that varied from 0.5 to 5 mm in thickness. Throughout

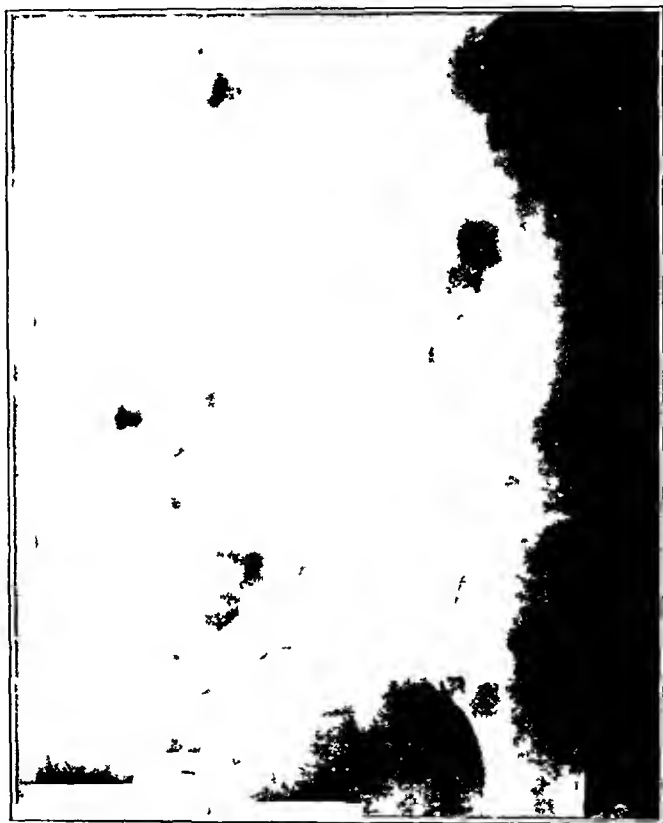


Fig 19 (case 6)—Roentgenogram of the hip showing a diffuse reduction in density of the head with large circumscribed and markedly rarefied areas scattered in it.

the whole circumference, the articular cartilage was intact and adherent to the underlying narrow strip of subchondral bone. In the outer portion of the spongiosa corresponding to the areas of markedly reduced density in the roentgenogram were areas made up of brownish, broken-down fatty tissue of putty-like consistency. Embedded in these areas were small, fine fragments of bone.

*Microscopic Appearance*—The articular cartilage as a whole was intact although slightly thinned over the superior surface (fig 22). Only a few of the cartilage cells were missing, and in their lacunae, small, dark bodies remains of the cartilage cells, were still seen. More normal cartilage cells were



encountered around the fovea. The thinning of the articular cartilage in the superior portion of the head appeared to be due partly to replacement of the superficial layer by the pericondral fibrous tissue, and to a greater extent to the invasion of the articular cartilage from the subchondral fatty marrow and vascular spaces, with the formation of huge and well defined cavities in it. These spaces contained fat, blood vessels and a few multinucleated giant cells, and were

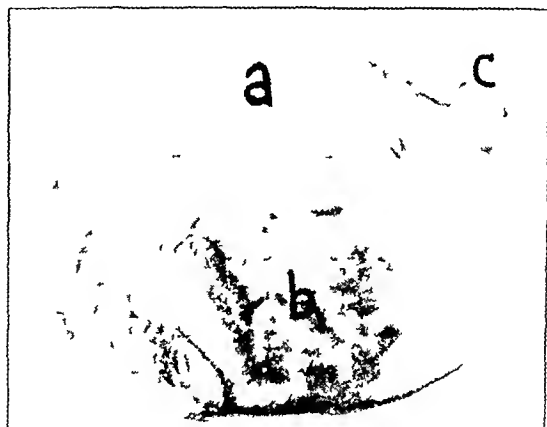


Fig 20 (case 6) —Appearance of the femoral head showing smooth, whitish articular cartilage (a), thin, bluish cartilage (b) and ligamentum teres (c)



Fig 21 (case 6) —Photomicrograph of a section of the femoral head showing marked loss of the bony trabeculae and absorption in articular cartilage

partially lined by narrow strips of newly formed bone. Islands of newly formed hyaline cartilage were seen about these chondral marrow cavities (fig 23). They appeared to arise from the deeper layer of the perichondrium and surmounted the newly formed lamellar bone in places. The cartilage cells were found singly or in twos enclosed by a capsule and separated by a bluish homogeneous matrix. As a whole, the thin layer of subchondral bone at the osteochondral margin was

preserved and appeared normal, so that, though markedly thinned out, the articular cartilage remained intact and attached to the spongiosa. At the fovea, remnants of the round ligament with a few slightly dilated blood vessels were seen. A small amount of osteoid tissue was laid down about some of the bony trabeculae near the vessels in this region. The brownish, granular material that nearly filled the spongiosa was made up of fat, poorly cellular marrow infiltrated with thin-walled blood vessels and a few monocytes. Embedded in this marrow were occasional small fragments of bony lamellae which showed well staining nuclei. This evidently was the picture of high grade atrophy.

*Summary*—Summarizing the case, one finds

- 1 Four years old intracapsular fracture of the neck of the femur with erosion of the neck fragments
- 2 Roentgenogram showing marked diffuse decrease in density of the head as well as of the pelvis and shaft



Fig 22 (case 6)—Section of the superior portion of the articular cartilage invaded by the subchondral marrow and vascular spaces,  $\times 60$

- 3 Living but markedly atrophied head with slight formation of osteoid tissue about the fovea
- 4 Presence of the ligamentum teres containing blood vessels
- 5 Marked thinning of the superior portion of the articular cartilage due partly to replacement by perichondral fibrous tissue and partly to invasion by the subchondral marrow and vascular spaces
- 6 Formation of islands of new hyaline cartilage and lamellar bone in place of the old articular cartilage

#### CASE 7 (PARTIALLY NECROTIC HEAD)

Case 7 is cited to show that a part of the head may remain alive and that the weight bearing portion of surviving articular cartilage of a

severely atrophic femoral head may be so thinned out by invasion and replacement from the subchondrial fatty marrow that actual honey-combing of the articular cartilage occurs. The area becomes filled with marrow tissue in which strips of lamellar bone surmounted by new articular cartilage is later formed.

A woman, 52 years of age, three years before examination fell on her left hip and felt something give way. On attempting to rise, she found the left lower



Fig 23 (case 6) —Section of newly formed surface showing perichondrium (a), newly formed hyaline cartilage (b), new lamellar bone (c), vascular spaces (d) and remnant of the calcified portion of the old articular cartilage (e). Reduced from a magnification of  $\times 160$ .

limb useless and markedly painful. She was told that she had a fracture of the neck of the left femur and was taken to a hospital, where the leg was immobilized and traction applied for five weeks. At the end of this period, she was allowed to go about with crutches although she could hardly bear weight on the hip on account of pain. A roentgenogram of the left hip taken on the day of examination

revealed an old ununited intracapsular fracture of the neck of the left femur with separation of the fragments and absorption and erosion of the neck (fig 24). The head, which was found to be in the acetabulum, showed a marked diffuse decrease in density, except for a small region in its superior portion, which revealed almost no reduction in density. There was an irregular area of increased density in the central portion of the infratrochanteric portion of the shaft, the cause of which was not known.

A Whitman reconstruction operation was performed three days after the examination. At operation, the neck fragments were found eroded away and the greater trochanter displaced upward to the level of the superior acetabular margin. The head was markedly adherent to the acetabulum by means of thick fibrous tissue which was attached to the fracture surface. In removing the head, the fibrous adhesions and the ligamentum teres, which could hardly be identified, had to be cut.

*Macroscopic Appearance of the Excised Head*—The femoral head showed an almost normal spherical shape, except for a large depression at the superior



Fig 24 (case 7)—Roentgenogram of the hips. Note the markedly diffuse decrease in density of the head of the left femur with a small dense area at its superior portion and the calcification at the upper third of the femoral shaft.

surface about the fovea (fig 25A). This depression was due to a loss of the articular cartilage and of the underlying spongiosa. It measured 2.5 cm in diameter and 1.5 cm in depth. A mass of fat with a few minute pieces of bone lying loosely in it was seen occupying this region. The articular cartilage about the defect was thin. It was made up of irregular and discrete areas of glistening, bluish cartilage, which extended to the outer circumference of the head, where they merged into the clear, whitish, shiny articular cartilage. There was a dense unchanged island of bone 1 by 0.5 cm along the superior articular surface as shown in figure 25B. The fracture surface of the head showed a layer of thick fibrous tissue, which was adherent to it, while that of the lower fragment was covered by dark red, granular tissue in which small fragments of loose bone were embedded.

On being sawed, the head was found abnormally soft in places which cut with marked ease. The cut surface presented an articular cartilage that varied in thickness from 0.5 to 4 mm, and it also showed the erosion in the articular cartilage at the superior surface of the head. The center of the spongiosa was occupied by

fat in which lay small pieces of bone. Only about the fracture surface and at the osteochondral junctions did the masses of fat merge into the fine, fibrillary, whitish spongiosa, which appeared normal. Ordinary hematoxylin and eosin stains were made, as well as the scharlach R stain for fat.

*Microscopic Appearance*—As a whole, the head was alive and presented a picture of severe atrophy. In spite of marked thinning, the articular cartilage was continuous and adherent to the underlying narrow strip of subchondral bone, except at the superior portion about the fovea, where the head showed a marked loss of substance in both articular cartilage and spongiosa. In general, the cartilage cells were present and well stained. The articular cartilage about one of the osteochondral junctions had been completely replaced by fibrocartilage. Slight calcifications of the deeper layer of the rest of the articular cartilage could be noted. As in the other femoral heads that remained alive but became atrophic after the fracture, there was an outstanding change in the articular cartilage, which was present in a greater degree. This change started at the superior

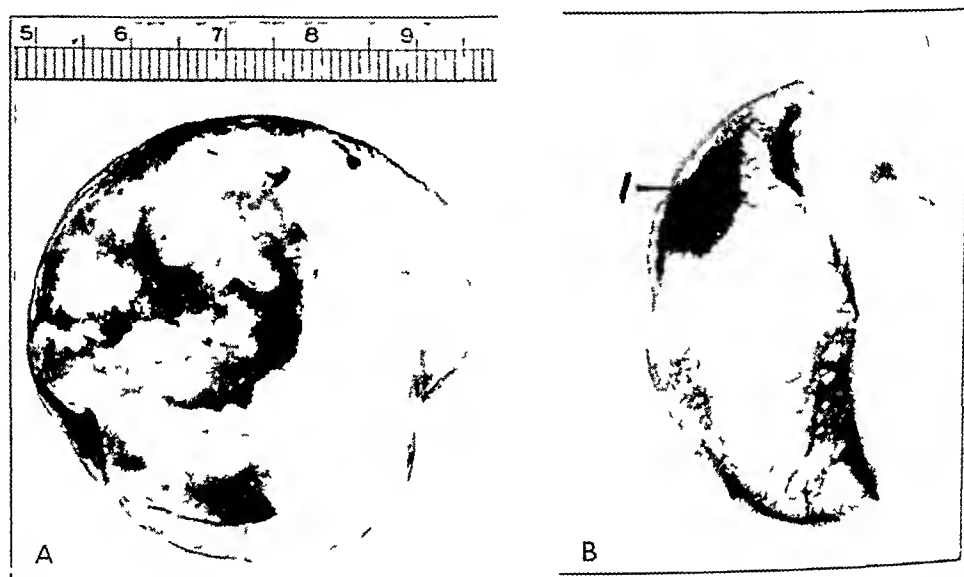


Fig 25 (case 7) —*A*, photograph of the excised head, and *B*, roentgenogram of a slice of the head showing atrophic living portion and small dense necrotic portion along superior articular cortex (1)

portion of the articular cartilage which was in contact with the acetabulum, and consisted in an invasion by the subchondral fatty marrow and vascular spaces, which resulted in the formation of marrow cavities in the cartilage layer (fig 26). With the progress of the atrophy as in this case, and the subsequent dilatation of the subchondral marrow cavities, there was also a corresponding enlargement of these chondral marrow spaces. The cavities contained fat, a few red blood cells, monocytes, osteoblasts and occasional multinucleated giant cells. The process extended from the superior portion of the articular cartilage down and along the outer circumference of the head, replacing and dissecting the cartilage as it advanced into distinct and fairly separated layers. Along the margins of the intrachondral spaces, strips of newly formed lamellar bone were seen. The part of this layer of new bone which overlay these spaces spread out simultaneously with the enlargement of the latter, and assumed the general appearance of subchondral bone. In places, small newly formed bony projections which were parts of the marginal lamellar bone of the chondral marrow cavities, were seen as it budding off

from the newly formed subchondral bone. Embedded in a matrix of fatty marrow and projecting down from the subchondral bone, these parts of the marginal bony lamellae became new bony trabeculae. The superficial layer of the old and split articular cartilage soon disappeared and became replaced by a more or less dense fibrous tissue which was slightly vascular, and which subsequently overlay the newly formed subchondral bone. Along their junction, distinct calcification of the deeper layer of the fibrous tissue was noted. In this region, the fibrous tissue assumed an embryonal appearance and, in places, gave rise to islands of newly formed cartilage.

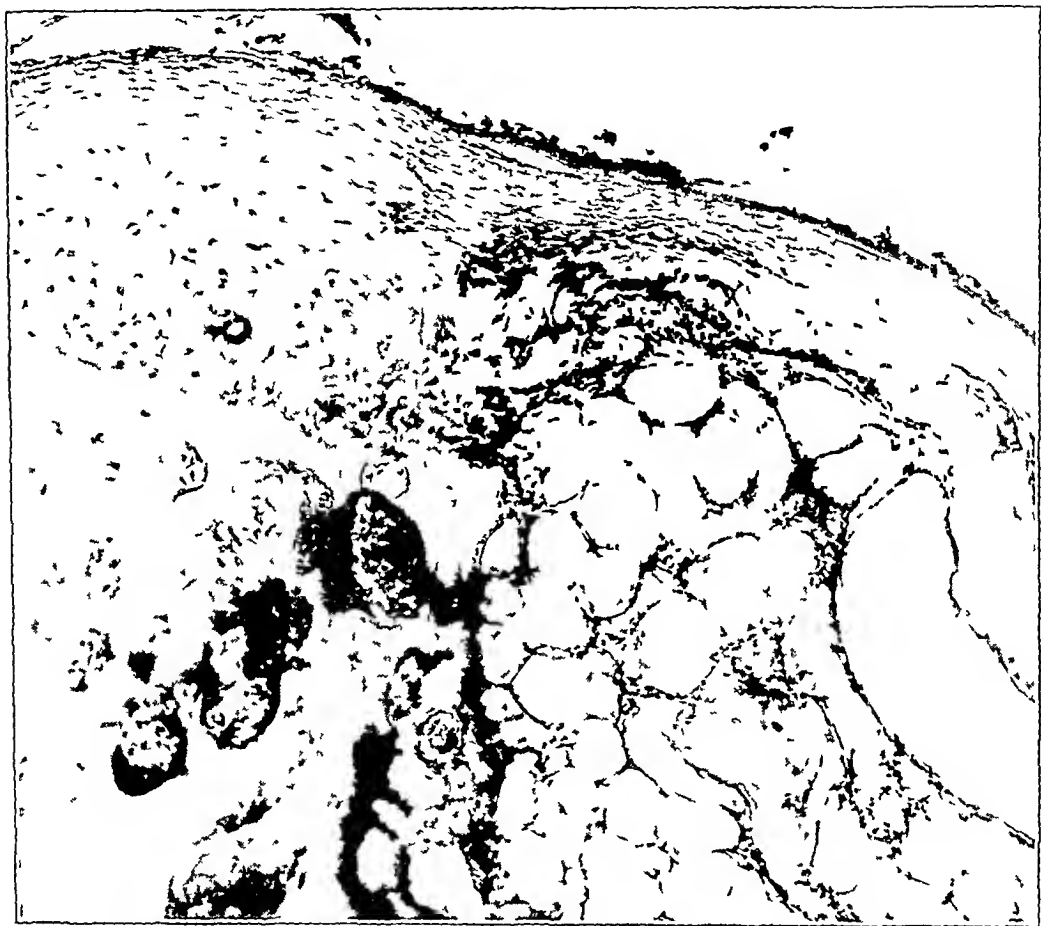


Fig 26 (case 7) —Section of the superior portion of the articular cartilage showing invasion by the subchondral marrow and vascular spaces with replacement of the old cartilage and formation of new cartilage and lamellar bone. Reduced from a magnification of  $\times 160$ .

cells lying in a bluish, homogeneous matrix. These islands of new cartilage cells occupied the sites of the thin, bluish cartilage nodules about the erosion as seen in the gross specimen. It was therefore evident that throughout this area an active reparative process was taking place. And this consisted in the formation of a new layer of articular cartilage with a slightly calcified deeper portion, surmounting newly formed subchondral bone and spongiosa in the region of the old articular cartilage. This histologic appearance makes it likely that a refilling and disappearance of the erosion in an atrophic head occurs by a complete reformation

sooner or later, of the cartilaginous and osseous elements of the femoral head. This is well illustrated by the case reported by Heine, as will be briefly described later.

The spongy portion of the head was made up of markedly dilated marrow spaces filled with fat, a few blood vessels and occasional monocytes. Its bony trabeculae everywhere showed well staining bone cells. The dense island along the superior articular cortex consisted of necrotic bone with its original trabeculae and bony cortex unaltered. It was bordered by fibrous tissue along its deep surface which was producing slight absorption of the dead trabeculae. Along the cortex it was surmounted by a necrotic and markedly calcified articular cartilage which showed superficial erosion and replacement by fibrous tissue. This small area presented a picture of necrosis without substitution as contrasted with the marked atrophy which the living portion of the head had undergone. At the center of the living portion the trabeculae were represented only by a few small detached fragments of living bone. At the osteochondral junctions and along the fracture surface, however, the bony lamellae showed a slight increase in size and number. A thick layer of fibrous tissue was found attached to the eroded fracture surface of the head, and a cortex of newly formed bone surrounded by osteoblasts and slightly fibrous and vascular marrow was seen along its whole extent. One must consider the possibility of complete necrosis of the head with creeping substitution of all except the dense area in the upper portion, but partial necrosis seems the more plausible explanation.

The distal fragment, the upper spur of which was clipped off, also showed a picture of marked erosion, necrosis and absorption. The cancellous spaces, especially those about the fracture surface, were hugely dilated and contained slightly loose and vascular connective tissue which was infiltrated with fat, degenerated red blood cells and occasional small and necrotic fragments of bone. On being traced laterally, the spaces soon showed rich collections of multinucleated giant cells (osteoclasts) which had markedly absorbed and reduced the necrotic cortex to a thin layer of bone. No evidence of new bone formation was seen. Further down the neck, however, a few well staining bone cells could still be discerned about the haversian canals, thus giving a picture of partial necrosis as seen in areas with diminished blood supply.

*Summary*—The case may be briefly summarized.

1 Three years old intracapsular fracture of the neck of the femur with erosion and separation of the neck fragments.

2 Roentgenograms showing a marked decrease in density of the fragments with absorption and erosion of the neck.

3 Largely living and severely atrophic femoral head with a necrotic area of bone and cartilage at the superior portion.

4 Presence of the ligamentum teres and of adhesions to the eroded neck surface.

5 Invasion of the articular cartilage by the subchondral fatty marrow with erosion and loss of substance of the head at its superior portion.

6 Active formation of new articular cartilage and bone about the site of the erosion.

7 Necrosis with active absorptive process in the femoral neck.

#### COMMENT ON CASES IN WHICH HEAD FRAGMENT REMAINED ALIVE

It is clear from cases 5, 6 and 7 that, after a femoral head has been separated from the distal fragment following an intracapsular fracture of the neck of the femur, it may still be preserved and its vitality maintained by adequate nutrition from the vessels of the round ligament.

This was further unequivocally shown in the recent studies and investigations of Frangenheim,<sup>6</sup> Schmorl<sup>4</sup> and Hesse.<sup>15</sup> Schmorl, for instance, found that in only one of thirty-four such cases was there a total necrosis of the femoral head. He cited a case in a young man in which, in spite of the complete destruction of the capsule around the femoral neck, the whole head was sufficiently nourished by the vessels of the ligamentum teres to prevent necrosis. Even in old age, these vessels may continue to supply the femoral head adequately. Nussbaum showed this in a person 64 years of age. Here he also found an extensive anastomosis between the arteries of the ligamentum teres and those of the femoral neck. Frangenheim showed, in a man 85 years of age, large vessels in the round ligament which furnished sufficient nourishment to preserve the femoral head.

From the descriptions of the specimens (cases 5, 6 and 7), it may be noted that the head, except in case 7, in which a small necrotic area was present, had remained alive, as shown by the presence of living cartilage cells in the articular cartilage and normal-staining bone cells in all the lamellar systems of the spongiosa. This fact more than suggests the presence of sufficient circulation and nutrition from the blood vessels of the ligamentum teres. But, owing to the separation of the fragments and subsequent throwing of the head out of function, the latter undergoes an atrophic change, which consists of a diminution in the number and size of the bony trabeculae, and a dilatation of the marrow cavities which become filled with fatty marrow. The degree of atrophic change bears a direct relation to the duration of the functional loss. As a rule, traumatic influence on such living structures is not as readily productive of damage as in a necrotic head. This, in part, explains the absence of gross erosions of the cartilage and bone in the first two cases. Such erosions are altogether absent in a less atrophic head, as in early cases. Even early in the process, certain histologic changes involving the articular cartilage and starting at its superior portion where the femoral head is in contact with the acetabular wall can be well recognized. These consist in an invasion of the deeper layer of the cartilage by the subchondral fatty marrow and vascular spaces, presenting a picture of marrow cavities in the cartilage layer. These medullary spaces contain fatty and slightly fibrous marrow, mixed with lymphoid structures, red blood cells, osteoblasts and a few large multinucleated giant cells, which are seen to proceed from the subchondral region. A similar process is frequently encountered at the osteochondral junction, but for which no definite explanation has been given judging from the prevailing and conflicting views. Importance has been attached to this process by Pommer<sup>16</sup> who thought it

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16 Pommer, G. Zur Kenntnis der Ausheilungsbefunde bei Arthritis deformans besonders im Bereich ihrer Knorpelursuren nebst einem Beitrag zur Lacunaren Knorpelresorption, *Virchows Arch f path Anat* **219** 261, 1915



to be a characteristic change in the early stage of genuine arthritis deformans. Recently, however, after an examination of 15 000 joints, Heme<sup>17</sup> came to the conclusion that it is not specific for arthritis deformans, as it is also commonly seen in physiologic resorptive processes.

It must be admitted that such a process in the articular cartilage accompanies atrophy of the head, and this naturally raises the question whether, like the bone, cartilage with its secondary invasion by the subchondral vascular spaces may also undergo atrophy following disuse of the part. Such an association is so constant and striking that a study is being made as to its real significance. It may be looked on as both an absorptive and a formative change of the articular cartilage which is associated with, and perhaps caused by, the atrophy. Although ordinarily trauma to a living but atrophic femoral head is not productive of damage, nevertheless, where this atrophic change has advanced to a marked degree and the replacement of the articular cartilage by the subchondral marrow is extensive slight injury, as the constant pressure against the acetabulum may cause destruction or indentation of the remaining, thin articular cartilage at the superior surface of the head. Such a secondary absorptive change in the head occurring mainly at the point of contact bears a certain similarity to the not infrequent pressure atrophy. Kaufmann<sup>18</sup> stated that under the influence of continuous pressure, even from a soft and elastic substance, increased resorption of bone both lacunar and smooth, occurs with resulting atrophy. As an example may be mentioned the erosion of bone by aneurysms, particularly those of the aorta, with disappearance of portions of the vertebrae, the ribs and the sternum.

The origin of the multinucleated giant cells and the rôle they assume in atrophy are still disputed questions. Pommer<sup>19</sup> thought that they were derived from the endothelial cells of the blood vessels. With the slowing of the blood flow and the rise of blood pressure because of the lack of functional demand on the circulation, injury of the vessel walls from insufficient nutrition occurs which results subsequently in the formation of osteoclasts. It may also be assumed that owing to generalized atrophy the bone building cells become atrophic and consequently their functional capacity becomes reduced. This atrophy then leads to a decrease in osteoblastic activity, and hence the normal relation between bone formation and absorption is disturbed. As a result of this insuffi-

17 Heme, I. Ueber primäre chronische Gelenkerkrankungen, *Ztschr. f. orthop. Chir.* **49** 7, 1928.

18 Kaufmann, E. *Spezielle pathologische Anatomie*, Berlin, G. Reimer 1896, vol. 1, p. 830.

19 Pommer, G. Ueber Osteoporose ihren Ursprung und ihre differentialdiagnostische Bedeutung, *Arch. f. klin. Chir.* **136** 1, 1925.

ciency of the osteoblasts and the presence of the multinucleated giant cells, replacement and absorption of the cartilage and bone occur. Although the accuracy of this explanation is obviously open to criticism, nevertheless the histologic appearances more than suggest that the invasion with subsequent replacement of the articular cartilage by the subchondral marrow is partly due to phagocytic activity.

With the advance of the atrophic process in the spongiosa, a simultaneous and progressive dilatation of these chondral cavities and perhaps increased activity of the phagocytes appear at the expense of the cartilage. The remaining articular cartilage overlying these marrow spaces may be reduced to a sheet so thin that actual breaks may be encountered (case 6) or definite erosions of the cartilage with replacement by honeycomb-like fatty marrow spaces and subsequent formation of new articular cartilage may be seen (case 7). If the atrophy advances even further numerous new lamellae of bone having a new cartilaginous articular surface replacing the whole of the old articular surface of the head may be encountered. This is seen to start at the portion of articular cartilage which is in contact with the acetabulum and later extends along the outer circumference of the head (case 7) and leads to a complete reformation of its articular surface. A case reported by Heine<sup>20</sup> is cited to serve as illustration.

The patient was a woman, 46 years of age, who sustained a complete intra-capsular fracture of the neck of the right femur with a resulting pseudo-orthosis for five years. A roentgenogram of the right hip showed separation of the fragments and a considerable diffuse decrease in the density of the head of the femur. At autopsy, the head was found adherent to the acetabulum by the ligamentum teres with thick fibrous tissue attached to the fracture surface. On microscopic examination, the entire head was found well preserved in spite of the severe atrophy. There was good staining of the cell nuclei everywhere, and no signs of necrosis could be detected. In the region of contact between the head and the acetabulum, an entirely new articular surface had formed on both sides. A new layer of bone having a new cartilage covering was found over the old articular cartilage about the region of the fovea. Here, the old articular cartilage had completely disappeared in some areas and in its place a layer of newly formed lamellar bone was seen. The old articular cartilage near the fovea was honeycombed by dilated medullary cavities which showed intervening narrow walls of bluish-white hyaline cartilage. These medullary spaces were filled in part by fatty marrow and in part by a fibrous and lymphoid tissue which contained a number of multinucleated giant cells. The cells of the old articular cartilage at the outer circumference of the head showed marked proliferation.

Although secondary degenerative change in a separated and necrotic femoral head is the rule nevertheless in a separated head that remains alive following the fracture no such permanent change occurs. The

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<sup>20</sup> Heine, I. Zur Kenntnis der Hüftgelenkveränderungen bei veralteten subkapitalen Schenkelhalsfrakturen, *Zentralbl f Chir* 51 1390, 1924.

only change that occurs in the articular cartilage of the living head is the encroachment on it of the subchondral fatty marrow. A physiologic resorptive process commonly seen even in normal joints, it invariably disappears rather promptly or readily leads to a reformation of the articular surface. Its disappearance is especially hastened on resumption of function of the part, and this is particularly true in the early cases in which no gross erosion of the articular cartilage has as yet taken place. If, however, the atrophy of the head has advanced to a marked degree, as in cases of more than three years' duration, with actual erosion and with complete disappearance of the articular cartilage and underlying spongiosa over its superior portion, a simultaneous formation of new articular cartilage and subchondral bone may result, with complete replacement of the old articular cartilage of the head. Unlike the secondary degenerative, absorptive and progressive change in a necrotic head, therefore, this change in a living head is transitory and reparative and ends in the formation of new articular cartilage and bony trabeculae.

There are also roentgenologic observations which are important, but which have received no attention. If the roentgenogram, however, is considered together with the pathologic changes taking place in the femoral head and neck, they will be found to agree. Except in early cases, in which tissue changes in either the head or neck have not as yet occurred, the roentgenogram is of great significance in determining the nutritional state of the head and neck of the femur. The basic facts underlying the roentgenologic interpretation are as follows: decrease in the density of a varying degree is always noted in the heads that remain alive but which become atrophic after the fracture. A head, however, that becomes necrotic following the fracture, retains its normal density for a considerable time afterward. When the necrotic head is subsequently revascularized, this is shown by a corresponding decrease and irregularity in density. New bone formation in the secondarily vascularized regions is indicated by irregular, fine densities scattered in these areas. A necrotic head that is secondarily vascularized may after a long time show as much reduction of density as an atrophic living head. But the former may usually be distinguished from the latter by its patchy appearance and simultaneous marked absorption and distortion of normal contour.

#### REUNION OF THE FRAGMENTS

When the fragments after a complete intracapsular fracture of the neck of the femur remain in good apposition or are impacted, the head whether alive or necrotic, may unite with the distal fragment. A fibrous or bony consolidation may follow, depending on the duration of the apposition of the fracture surfaces.

CASE 8 (NECROTIC HEAD)

A case of twenty-four days duration may be cited to indicate a necrotic head entering into fibrous union with the distal fragment. A beginning erosion with fibrous tissue replacement of the articular cartilage about the fovea was also noted. Although the ligamentum teres was present there was no sign of newly formed vessels or connective tissue invading the head from it.



Fig. 27 (case 8)—Cut surface of the upper third of the femur removed at necropsy showing ligamentum teres (*a*), fracture line (*b*), area of impaction (*c*) and necrotic but intact articular cartilage (*d*).

The patient was a man 80 years of age. He slipped and fell on his left hip which resulted in disability. He was immediately taken to a hospital. A roentgenogram taken the next day showed an impacted intracapsular fracture of the neck of the left femur. He was put to bed, where he remained until his death, twenty-four days after the injury. The upper third of the femur was removed at autopsy.

*Macroscopic Appearance of the Specimen*—The fresh cut surface of the specimen showed a transverse fracture of the proximal third of the neck of the femur with impaction of the fragments in the lateral third of the fracture line (fig. 27). The periosteum of the neck was intact on the mesial side. A portion of

the ligamentum teres was attached to the head. The articular cartilage was smooth, clear and intact, except at the region of the fovea, where it was slightly eroded. At about the center of the head there was a darkly stained oval area which extended down into the neck across the fracture line to the distal fragment. The rest of the interior of the head was yellowish and uniformly trabeculated. There was slight mobility between the fragments.

*Microscopic Appearance*—The round ligament was represented by a narrow strip of slightly dense avascular connective tissue which did not penetrate the spongiosa. The articular cartilage about this region was very slightly eroded and replaced by fibrous tissue which extended from the region of attachment of the ligamentum teres to the head (fig 28). Except for this erosion, the articular cartilage as a whole, although necrotic, was intact and adherent to the underlying subchondral bone. Most of the cartilage spaces, especially around the fovea, were empty. The remaining cartilage cells stained rather poorly. There was marked calcification of the deeper layer of the articular cartilage. The bony lamellae were

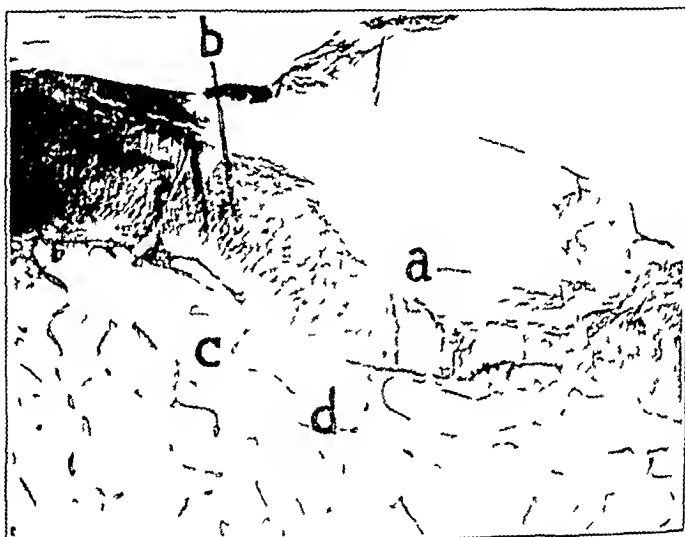


Fig 28 (case 8) —Section of the fovea showing the absence of vascularization of the spongiosa from the ligamentum teres,  $\times 60$

necrotic and lay except in the dark area in a matrix of degenerated marrow, which was practically acellular and avascular and contained large empty spaces. No attempt at replacement of these necrotic bony lamellae by fibrous connective tissue was seen. However, in the oval area extending for a distance of 2 cm from the fracture line up into the neck and base of the head, and in the region of contact between the fragments, active absorptive and regenerative changes were encountered. Here the necrotic bony trabeculae of the head were embedded in a highly vascularized connective tissue rich in blood vessels, red blood cells, and containing a few osteoblasts and multinucleated giant cells. At the borders of some of the necrotic bony lamellae newly formed bone surrounded by numerous osteoblasts was seen. Active lacunar absorption of bone was taking place in the same region. The vascularized tissue bridging the fracture line appeared to proceed from the marrow of the living distal fragment. The region of impaction was filled with small fragments of dead bone.

As in an ununited intracapsular fracture of the neck of the femur the necrotic portion of the distal fragment presented a striking picture of slight formative and simultaneously active absorptive processes. Throughout the region of contact

between the fragments, a broad band of highly vascular connective tissue was seen extending from the cancellous spaces of the neck into the head. In this region a network of small newly formed bone surrounded by osteoblasts was seen about the fracture surfaces (fig 29). At the periphery of the neck, however, a picture of partial necrosis of the bony lamellae was encountered. Here, the bone cells were found only about the haversian canals and were absent in the compact portion of the bone and the intermediate lamellae (fig 30). An active lacunar absorption of these partially necrotic bony lamellae was also taking place.



Fig 29 (case 8) —Photomicrograph of section showing the region of contact of the fragments: original bony lamella of the distal fragment (a), fracture line (b), proximal fragment (c), rich network of newly formed bone (d) and osteoblasts (e). Reduced from a magnification of  $\times 160$ .

*Summary*—The case may be summarized as follows:

- 1 Impacted intracapsular fracture of the femoral neck of twenty-four days' duration with total necrosis of the head and partial necrosis of the neck.
- 2 Presence of the ligamentum teres, but no signs of revascularization of the head from it.

3 Beginning erosion of the articular cartilage about the fovea with fibrous tissue replacement

4 Slight replacement of the necrotic bony lamellae and formation of new bone in the head at the region of contact with the distal fragment

5 Extension of vascular connective tissue from the distal fragment across the fracture line into an adjacent portion of neck and head. No sign of vascularization of the necrotic head through the intact periosteum along mesial side of fracture



Fig 30 (case 8) —Periphery of the distal portion of the neck showing necrosis and marked lacunar absorption of the bony trabecula with slight formation of new bone. Reduced from a magnification of  $\times 160$

6 Partial necrosis, slight formation of new bone and active bone absorption in the distal fragment of the neck near the fracture line

*Comment* —Here one has an early case of intracapsular fracture of the neck of the femur in which the fragments are in good apposition. It may be noted that in this case there was no attempt at revascular-

ization of the necrotic head from the region of the ligamentum teres. The beginning stage of bony consolidation which mainly proceeded from the partially necrotic neck was seen. With this there were also early signs of organization of the necrotic head in its secondarily vascularized region.

#### CASE 9 (NECROTIC HEAD)

If a necrotic head such as that described in case 8 is allowed sufficient time in good apposition with the distal fragment, a complete osseous consolidation may result. Case 9 is cited to indicate this bony union.

The patient was a woman 49 years of age. One day before examination, she fell on her left hip, and because of the subsequent pain and disability in it, she had to be carried to her bed. Roentgen examination of the hip on the same day showed an intracapsular fracture of the neck of the femur with separation of the fragments. On the next day, a bone pegging operation, using a beefbone peg, was performed. The ligamentum teres was not identified. The cavity of the joint was found filled with bloody fluid. The patient was placed in a long plaster of paris spica, in which she remained for nearly three months. The cast was then removed, and passive movement of the leg was instituted. She was then allowed to be up and about with the aid of crutches. The roentgenogram of the hip taken nearly four months after the operation showed bony healing of the fracture (fig 31 A).

Eight months after the operation, the patient began to have pain in the left hip. Roentgen examination at this time showed an almost normal density of the head, as is regularly seen in a necrotic head, and slight irregularity of its weight bearing portion (fig 31 B). The neck revealed a slight diffuse decrease in density. The bone peg did not show any change. Because of the persistent pain in the left hip, an operation was performed four months later for the removal of the bone peg. At this operation, the fracture was found to be solidly healed. The patient subsequently passed an uneventful convalescence and went on to recovery with almost perfect use of her left leg until a year after the second operation (nearly two years after the bone pegging operation), then she started to complain again of pain and disability of the same hip (fig 31 C). A roentgenogram taken at this time showed absorption and collapse of the femoral head with separation of a portion of it at its weight bearing portion. Another operation was done for the removal of the collapsed portion of the head. This was found almost free in the joint, and on histologic examination it was seen to be made up of necrotic, although intact, articular cartilage and necrotic, unreplaced bony lamellae, which were embedded in a matrix of degenerated marrow.

It is of great interest to note that the portion of the peg about 4 cm. long lying in the trochanteric region of the distal fragment was markedly eroded and thinned and had a moth-eaten appearance, while the part included in the neck, 2 cm. long, was put slightly eroded (fig 32). The whole portion of the peg in the head, however, remained unchanged. This might be explained by assuming that a gradation of vascularization and vitality of the fragments after complete intracapsular fracture of the neck of the femur exists. Because of the absence of the ligamentum teres and its vessels, necrosis, loss in vitality and failure in revascularization of the head occur after the fracture, which accounts for the unchanged condition of the part of the peg in this region. In a similar manner, and following



the complete fracture, there results a destruction of the vessels along the neck, which are known to be the main source of nutrition for the femoral neck. Consequently, a diminution in vascularization and vitality with subsequent partial necrosis especially marked along the margins, as observed in histologic sections,



Fig 31 (case 9) —*A*, roentgenogram of the left hip taken four months after the bone pegging operation, showing healing of the fracture and practically no reduction in density of the femoral head. *B*, roentgenogram of the hip taken a year after the operation showing the dense head with beginning collapse of its weight bearing portion. *C*, roentgenogram taken two years and two months after the bone pegging operation. Note the separation of the collapsed and markedly dense portion of the head.

appears in it. The slight absorptive change at the corresponding part of the peg can well be explained by this condition of the neck. On the other hand, as the intertrochanteric region is supplied not only by the vessels running along the femoral neck, but also by a branch of the superior nutrient artery, the destruction of the neck vessels alone would result in little or no impairment of nutrition of this region. This accounts for the more or less normal vascularization and vitality of the trochanteric region of the distal fragment, as shown by the marked absorption and erosion of the peg included in it.

*Summary*—Summarizing the significant features, one has

- 1 Bone pegging operation performed one day after the injury, followed in four months by bony healing of the fracture
- 2 Necrotic head eight months after the operation, as shown by its normal density in the roentgenogram
- 3 Secondary collapse of the weight bearing portion of the head almost two years after the healing of the fracture
- 4 Eroded appearance of the bone peg within the trochanteric region, slight erosion of the part included in the neck and unchanged condition of the peg lying in the head

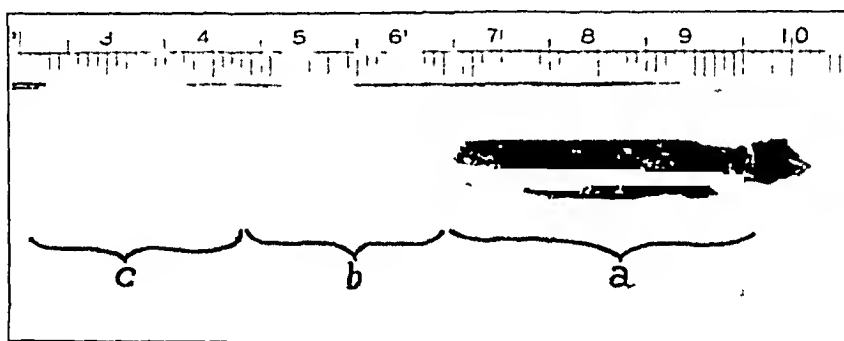


Fig. 32 (case 9)—Appearance of the removed bone peg showing portion included in the trochanteric region of the femoral shaft (*a*), part in the neck (*b*) and portion in the head (*c*)

- 5 Necrotic head as evidenced by the roentgenogram, by the absence of the ligamentum teres and by the appearance of the peg
- 6 A slight absorption of the neck

*Comment*—On the basis of the roentgenologic observations in separated femoral heads after fracture of the neck this femoral head can be considered with a high degree of certainty to have been necrotic. This is indicated by its diffuse normal density as seen in the roentgenogram made long after the bony union of the fracture took place. With this change in the head, it may be assumed that there were also varying degrees of necrosis with subsequent reduced vitality of the neck in this case, as suggested by the appearance of the bone peg included in it, by the diffuse rarefaction and erosion of the neck as seen in the roentgenograms and indirectly by the uniform histopathologic observation of necrosis (partial or com-

plete) in other femoral necks following such fracture. But in spite of the total necrosis of the head and the varying degrees of necrosis of the neck, bony healing of the fracture, although delayed, occurred within four months after the bone pegging operation. The collapse of the weight bearing portion of the head, which became evident two years after the bony union of the fracture, suggests that an efficient secondary vascularization of the necrotic head from the distal fragment, with complete organization and transformation had not appeared. Consequently, secondary degenerative change in the form of collapse, especially of the weight bearing portion of the head, took place. It is therefore justifiable to assume that healing of the fracture is possible from the slow ingrowth of callus from the necrotic and eroded neck. Although directly accountable for the healing of the fracture, the revascularization of the necrotic head from the distal fragment is a rather slow and weak process which invariably fails in thoroughly organizing and transforming it. As a consequence, the head remains necrotic and as in the case in which there is a necrotic and separated femoral head, it undergoes a secondary degenerative change. In this connection, and to show further the possibility of bony union of the fracture when the head is necrotic, a case reported by Axhausen<sup>13</sup> may be mentioned.

This occurred in a schoolboy, 16 years of age, who, ten months before examination, fell on his right hip. In spite of slight soreness in the hip, he was able to walk home with practically no disability. A roentgenogram taken at the time of the injury showed an impacted intracapsular fracture of the neck of the femur. The fracture healed, and the youth became able to make use of the limb without the least discomfort. Then, a few weeks before examination, he began to have pain and disability in the hip. The roentgenogram taken at the time of examination showed evidence of bony union, but with secondary collapse of the femoral head. The head, which was resected later, retained its normal density, as do other necrotic femoral heads. On microscopic examination, it was found to be totally necrotic, with replacement of the marrow at the upper osteochondral margin by a highly vascularized connective tissue which apparently extended from the distal fragment. The necrotic bony lamellae in this region showed lacunar absorption with simultaneous formation of new bone. This formation of new bone and reorganization were especially marked about the fracture surfaces and extended to the region of the epiphyseal cartilage. The articular cartilage was without nuclei. It was fissured and eroded for an area of 2.5 cm. in its superior portion exposing the underlying spongiosa.

#### CASE 10 (NECROTIC HEAD)

In the case of impacted intracapsular fracture of the neck of the femur now to be described, the roentgenograms showed that bony union occurred. But the proximal fragment was necrotic, as shown by the roentgenograms, and consequently it underwent a gradual disintegration and collapse in its weight bearing portion.

A man aged 55, fell on his left hip, Aug. 8, 1925. On account of the resulting pain and disability in this hip, he was unable to walk and had to be carried

home on a stretcher. The roentgenogram taken three days later showed an impacted intracapsular fracture of the neck of the femur. The extremity was put up in a long plaster of paris spica, in which it remained for thirty-one days. Roentgenograms taken at this time showed bony union of the fracture. After six weeks he walked on crutches and after four months he discarded them. However after six months the pain again became so severe that he resumed the use of crutches. A roentgenogram eight and a half months after injury showed slight collapse and irregularity in the weight bearing portion of the head and reduced density in the mesial portion of head fragment apparently from invasion of tissue from the distal fragment (fig 33 B).

The patient was again placed in a plaster of paris spica three months later, and remained in this cast for several weeks. Since then there has been marked limitation of motion and adduction deformity of the hip and pain on walking has been so great that he has continued the use of crutches. Roentgenograms were taken twenty months and three years and four months after the injury. They showed signs of a slowly progressive collapse of the weight bearing portion of the head and a progressive invasion and absorption of the rest of the head with replacement by irregularly arranged spongy bone. This is revealed in figure 33 C by the blotchy character of the shadow in the weight bearing portion and the reduced density in the lateral or nonweight bearing portion (*a*) projecting beyond the acetabular margin three years and four months after injury. It is evident that transformation was produced by tissue invasion from the distal fragment, but there appear to be no signs present by which one can say definitely that there was invasion from the round ligament. Figure 33 C also shows that a long time after union has occurred the density of the necrotic head which at first is unaltered may be as markedly reduced by invasion and transformation as is that of the living distal fragment and innominate bone by atrophy of disuse.

Case 10 shows that when the head becomes necrotic, bony union of the fracture may occur, but as a result of weight bearing the head may collapse and become markedly deformed before long transformation takes place, giving a poor functional result.

#### CASE 11 (NECROTIC HEAD)

In case 11, there was bony union in the presence of roentgen evidence of necrosis of the head fragments, but weight was not borne on the limb for eleven months and then only with the aid of canes for fourteen months. Transformation of the head was almost complete at the end of this time without collapse of the weight bearing portion and the hip was improving so that a fairly good functional result appeared to be in sight.

A man, aged 58, while boarding a street car, fell and forcibly struck his left hip on the step of the car. Because of pain and disability in the hip, he had to be aided to a stretcher, in which he was taken to the University of Chicago clinics. A roentgenogram showed complete intracapsular fracture of the neck of the femur with slight displacement of the fragments. With the patient under ethylene anesthesia, closed reduction was performed on the following day, and with the limbs abducted and internally rotated, a double, long plaster of paris spica was applied (fig 34 A). The lower fragment was displaced laterally about 0.75 cm. The cast was removed after ten weeks and another roentgen examination of the hip was made. It showed that the fragments were in apposition but the lower frag-

ment was externally rotated. There was moderate reduction in density of the fragment ends where they came in contact and the lateral half of the head fragment showed reduced density for 0.5 cm back from the fracture line. There was a spongy bony shadow across the fracture line. The rest of the head cast a shadow of the same density as that at the time of injury except in the region of

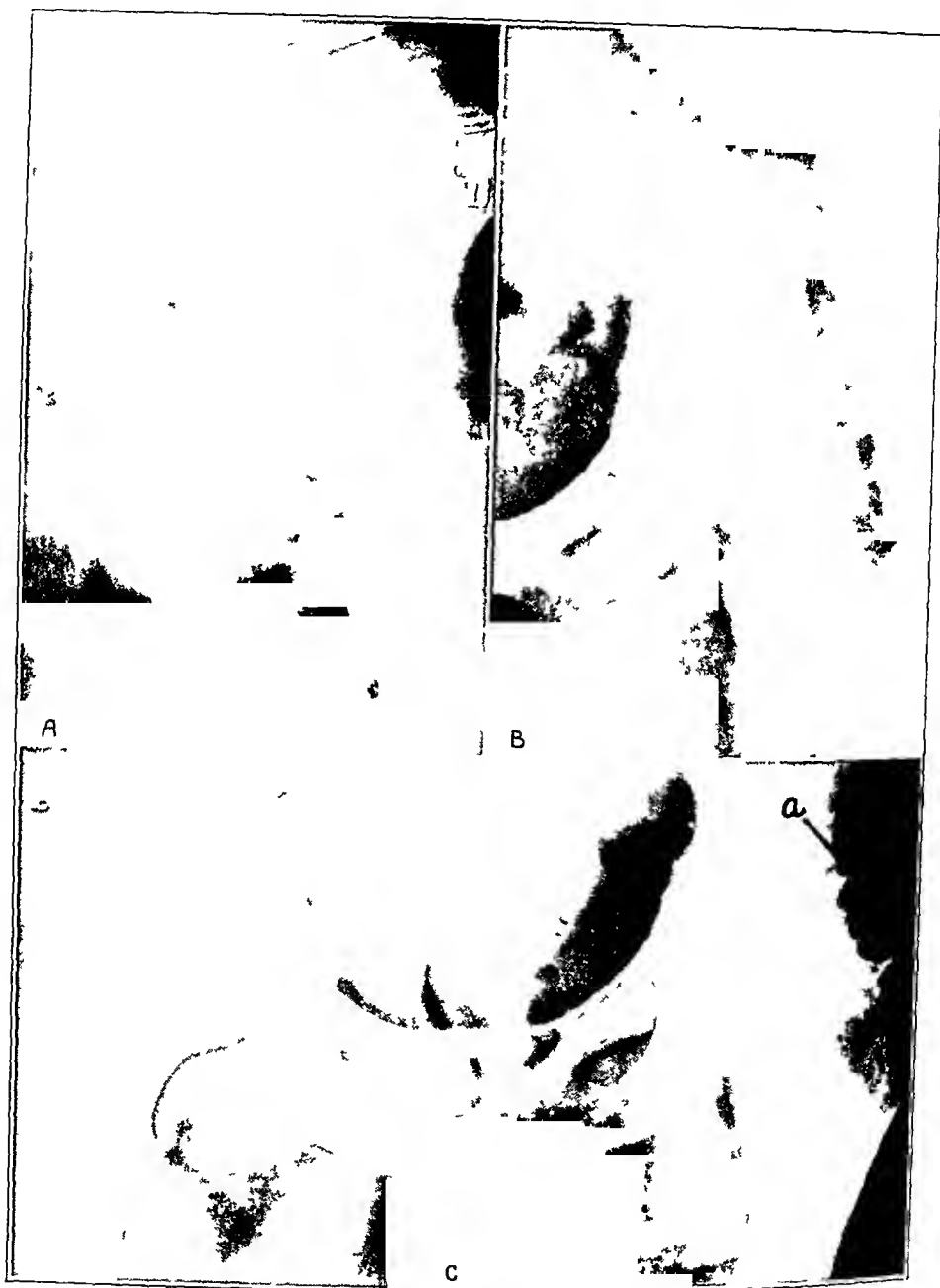


Fig 33 (case 10) —*A*, roentgenogram of the left hip taken three days after the injury. *B*, roentgenogram taken eight and one-half months after the injury. Note the dense femoral head and collapse of its weight bearing portion. *C*, roentgenogram taken three years and four months after the occurrence of the fracture. Note the marked absorption of the head. The outer circumference of the head which was nonweight bearing (*a*), although showing marked reduction in density, maintains a fairly normal contour. This portion shows that a necrotic area when not subjected to stress may after a long period be transformed and reduced in density without changing form.

the fovea where there was an oval shadow of reduced density 1 cm in its short diameter. The distal fragments and the innominate bone showed reduced density from atrophy of disuse. The interpretation is that the head became necrotic, that there was bony union of the fracture and that invasion and transformation of the dead head had begun, both from the round ligament and from the distal fragment across the healed fracture. The peroneus nerve was paralyzed and the limb

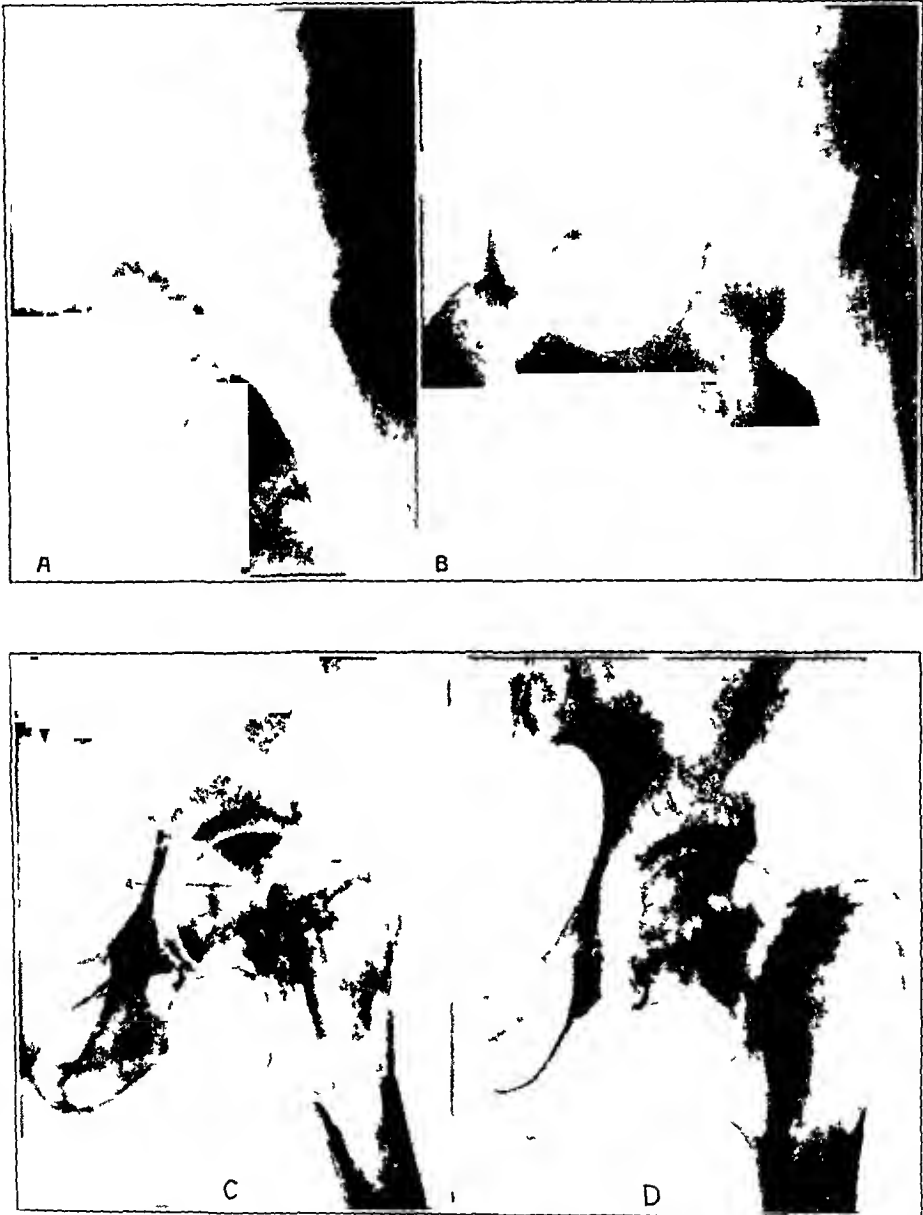


Fig 34 (case 11)—*A*, roentgenogram taken four days after repositioning of the fragments, which was performed on the day of the injury. *B*, roentgenogram taken three months after the injury, showing normal density of the head except for slight rarefaction about the fovea and repair of the fracture. *C*, taken five and one-half months after injury, shows a large area of irregular absorption and replacement of the head about the fovea (*a*). *D*, taken eleven months after injury, shows about three-fourths of the head transformed by invasion from both the fovea and from the distal fragment.

remained swollen for six months. The patient went on crutches for eleven months bearing no weight on the limb. Roentgenograms were taken four months, five and a half months, eleven months and fourteen months after injury showed a gradual transformation in the head proceeding largely from the fovea but to some extent from the distal fragment with irregular reduction in density, leaving a mottled spongy bone in more than four-fifths of the head but without any signs of collapse in the weight bearing portion of the cortex. The nonweight bearing portion laterally was replaced by bone casting a fainter and more even shadow than that in the weight bearing portion. The contour of the cortex of the head and the cartilage space of the joint are unaltered in outline.

The following case shows that when union occurs following intra-capsular fracture with necrosis of the head, the ultimate result may be fairly satisfactory, although a clinical picture simulating chronic osteoarthritis of the hip joint may remain after several years have elapsed.



Fig. 35 (case 11 X) —Roentgenogram taken five years after fracture of neck showing union with reorganization and cavitation of the head with slight collapse in the weight bearing portion, which is evidence that the head was necrotic.

#### CASE 11 X (NECROTIC HEAD WITH UNION AND FAIR FUNCTIONAL RESULT)

A woman, aged 62, fell on the right hip, which produced pain and disability. A roentgenogram taken immediately was thought to show no fracture. She got up after four days and walked with a cane. The hip gradually became more painful, so that after four weeks she began to use crutches. As there was no improvement at the end of four months, another roentgenogram was taken which was reported to show a healed fracture of the neck of the femur. The hip continued to be painful and the patient used crutches for three years, then a cane for one year, but for one and a half years has walked unaided. She was examined five and a half years after the injury at which time she walked with a slight limp and complained of pain and weakness in the joint on walking long distances. Examination showed 1 inch of shortening of the right leg with moderate limitation of rotation and abduction and 50 per cent limitation

of flexion in the hip. A roentgenogram (fig 35, case 11 X) showed a healed fracture with marked shortening of the neck of the femur and moderate *coxa vara*. The head shows evidences of marked reconstruction with the formation of large cavities and heavy irregular bony trabeculae in the weight bearing line. There is very slight collapse of the head along its weight bearing surface. The history and symptoms are consistent with an impacted fracture of the neck of the femur resulting in necrosis of the head and transformation and irregular replacement of the dead bone with little change in contour by ingrowing new bone under functional stimulation during the period when there was little or no weight bearing. The functional result was a fairly satisfactory one.

#### COMMENT ON CASES IN WHICH REUNION RESULTED DESPITE NECROTIC HEAD

It is therefore evident that necrosis of the head is not an absolute hindrance to bony union, as has been generally believed since the teachings of Kocher. Axhausen,<sup>12</sup> and later Bonn<sup>13</sup> thought that every complete intracapsular fracture of the neck of the femur results in necrosis of the head. The former stated that healing of the fracture in these cases is determined by the possibility of bridge formation between the fracture ends by the ingrowth of callus from the distal fragment, and revascularization and later organization of the head. It is beyond doubt that a bridge formation which at the start is made up of vascularized connective tissue and later callus may proceed exclusively from the distal fragment, as in Axhausen's case and cases 7, 9, 10, 11 and 11 X. In none of the cases here reported was there either histologic or roentgenologic evidence that callus forming in connection with blood vessels entering the necrotic head by way of the round ligament played a part in the healing of the fracture. Consequently, it must be concluded that when bony union occurs it is by way of new bone coming from the distal fragment. As Cornil and Coudray<sup>21</sup> have pointed out, there is necrosis of the cortex after fracture of any bone for a short distance back from the fracture line but that fact seems to play no more of a rôle in fractures here than elsewhere in the production of nonunion.

Organization of the necrotic head in case of union of the fracture proceeds from the tissues invading it from the distal fragment and in some cases from the round ligament. The rate of invasion of these tissues is variable, depending on the rapidity of union, the vascularity of the round ligament and the amount of functional stimulation from usage of the limb. As soon as union has occurred, usage hastens the rate of invasion of new tissue, of absorption of the necrotic tissue and of replacement by new-bone, bone-marrow and fibrous tissue. If there

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<sup>21</sup> Cornil, V., and Coudray, P. Du cal au point de vue expérimentel et histologique, *J de l'anat et de la physiol* 40 113, 1904.



is too much weight bearing early as in case 10, there may be collapse of the weight bearing portion and marked deformity of the head before replacement of the dead bone and cartilage takes place with a poor functional result. If, however, the head does not bear too much weight but there is functional stimulation by movement without walking on the limb, transformation may occur with little or no collapse of the head, as in cases 11 and 11 X. The end-result is a head that shows much internal derangement but which functions fairly satisfactorily. In case 11, much of the transformation was brought about by invasion from the round ligament, as judged by repeated roentgenograms over a period of fourteen months. The "secondary arthritis deformans" in four out of thirteen cases reported by Portwich<sup>22</sup> was probably due largely to necrosis of the head with disintegrative changes. Johansson<sup>23</sup> reported collapse and absorption in the head beginning one to two years after healing of the fractures.

#### SURVIVAL OF HEAD

When, however, the femoral head remains alive after the fracture and the fragments are in good apposition, bony union of the fracture will occur in the great majority of cases. Being alive, the head will maintain its configuration and will not undergo secondary degenerative changes even long after the fracture has healed. This is illustrated by cases 12, 13 and 14.

#### CASE 12 (LIVE HEAD)

Case 12 is cited to indicate prompt healing of a fracture with no displacement or following early reposition of the fragments. Because the head was alive, as shown by its diffuse rarefaction in the roentgenogram taken three months after the injury, it did not undergo secondary degenerative changes during the period of four years following the healing of the fracture.

The patient was a woman who at the age of 71 slipped and fell on her left hip. This resulted in marked pain in the hip and disability. The roentgenogram taken at the time of the injury showed an impacted intracapsular fracture of the neck of the femur with slight displacement of the fragments. An ambulatory splint was worn for one month (fig 36 A). The patient was then put in a cast for eight weeks, the cast was removed and another roentgen examination of the hip was made. This revealed bony union of the fracture with the neck in slight *coxa vara* (fig 36 B). The head retained its normal contour and appeared to be alive, as was disclosed by its diffuse decrease in density. She was seen again almost a year and ten months after the bony healing of the fracture. She had good use of the limb and could go about her ordinary work without discomfort. A roentgenogram of the hip at this time disclosed a head that had maintained its configuration and was

<sup>22</sup> Portwich, O. Ergebnisse der unblutigen Behandlung medialer Schenkelhalsfrakturen, *Deutsche Ztschr f Chir* **193** 145, 1925.

<sup>23</sup> Johansson, S. Ueber epiphyse nekrose bei geheilten Collumfrakturen. *Zentralbl f Chir* **54** 2214, 1927.

alive as was manifest in the slight diffuse decrease in density. In spite of the coxa vara, the hip had three-fourths normal range of motion.

The patient was seen three years and ten months after the injury because of cancer of the cervix uteri. There was almost normal function and slight limitation of motion in the left hip.

A roentgenogram (fig 36 C) showed the head still intact with bony trabeculae running into it from the distal fragment along the under surface of the neck. The



Fig 36 (case 12) —A, roentgenogram taken two days after the injury and a day after application of ambulatory splints. B, roentgenographic appearance of the left hip three months after the injury, showing a healed intracapsular fracture of the neck. C, roentgenogram taken three years and eight months after the healing of the fracture. Note the diffuse decrease in density of the head, its normal shape and slight coxa vara. D, roentgenogram of a section of the femur showing bony repair of the fracture and newly formed weight bearing trabeculae in the head.

patient died of the carcinoma four and one-third years after the injury and the upper end of the left femur was obtained at autopsy. The neck was markedly shortened and the head was in the position of coxa vara. The stump of a small round ligament projected from the fovea. The articular cartilage was markedly thinned and yellow gray about the margins and fovea, but there was a band in between which was only moderately thinned and bluish. A coronal section showed a very short neck with union by dense bone along the fracture line. There had been absorption and replacement of the impacted neck fragments with laying down of new supporting trabeculae extending from trochanter minor along the bottom of the neck and upward to the top of the head, as shown in a roentgenogram of a slice of the specimen (36 D). Microscopic sections were made of the head, neck and trochanters. The head was alive but markedly atrophic. The articular cartilage was thin and at the margins and about the fovea it was overgrown and largely replaced by connective tissue. Blood vessels were present in the stump of the ligamentum teres. There was a dense bony intermediary callus. No dead bone was seen in the region of either neck or head.

#### CASE 13 (LIVE HEAD)

Case 13 indicates a head that apparently remained alive after the fracture. Prompt healing occurred following early reposition of the fragments. The head preserved its normal configuration three years after the fracture had healed.

The patient was a woman, 68 years old. Three years before examination, she fell on her right hip striking it against a stone pavement. She had to be carried to her home in a stretcher because of the acute disabling pain in her hip. Roentgen examination made on the day of the injury showed complete intracapsular fracture of the neck of the femur with slight separation of the fragments (fig 37 A). With the patient under ether anesthesia, closed reduction was performed, and the leg was put in a double, long plaster of paris spica, in which it remained for eight weeks (fig 37 B). The cast was then removed and another roentgen examination of the hip was made. This disclosed a good alinement of the fragments and bony union of the fracture. The head maintained its normal shape and appeared alive, as shown by the diffuse reduction of its density. The last time the patient was seen was three years after the injury, she was then free from discomfort in the hip. The result was excellent, as shown by the normal range of motion of the hip and by the roentgenogram taken at this time, which revealed healing of the fracture with slight coxa valga. Judging by the criteria herein established the head was alive and preserved its normal configuration (fig 37 C).

#### CASE 14 (LIVE HEAD)

Case 14 indicates that when the head is alive and the fragments are in good apposition or impacted, a prompt healing of the fracture results in spite of failure to immobilize the hip. In such a case the head retains its normal configuration.

A woman, 54 years old, complained of slight soreness in the left hip which had been present for three months. Sixteen months before examination, she had fallen in the bathroom striking her hip against the edge of the bath tub. Every attempt to get up failed on account of the acute pain and disability of her hip. She was taken to her bed, where she remained for three days. The pain gradually

diminished in severity, and before the end of the week she was again able to be up and about. A roentgenogram taken two months after the injury showed a healed intracapsular fracture of the neck of the femur with impaction of the fragments (fig 38). Manipulation followed by weekly vigorous massage was carried out for five weeks. After this time, the patient had increasing relief from discomfort until three months ago, then she again began to have slight soreness in the hip. Fearing that she might have a deforming arthritis in the hip,

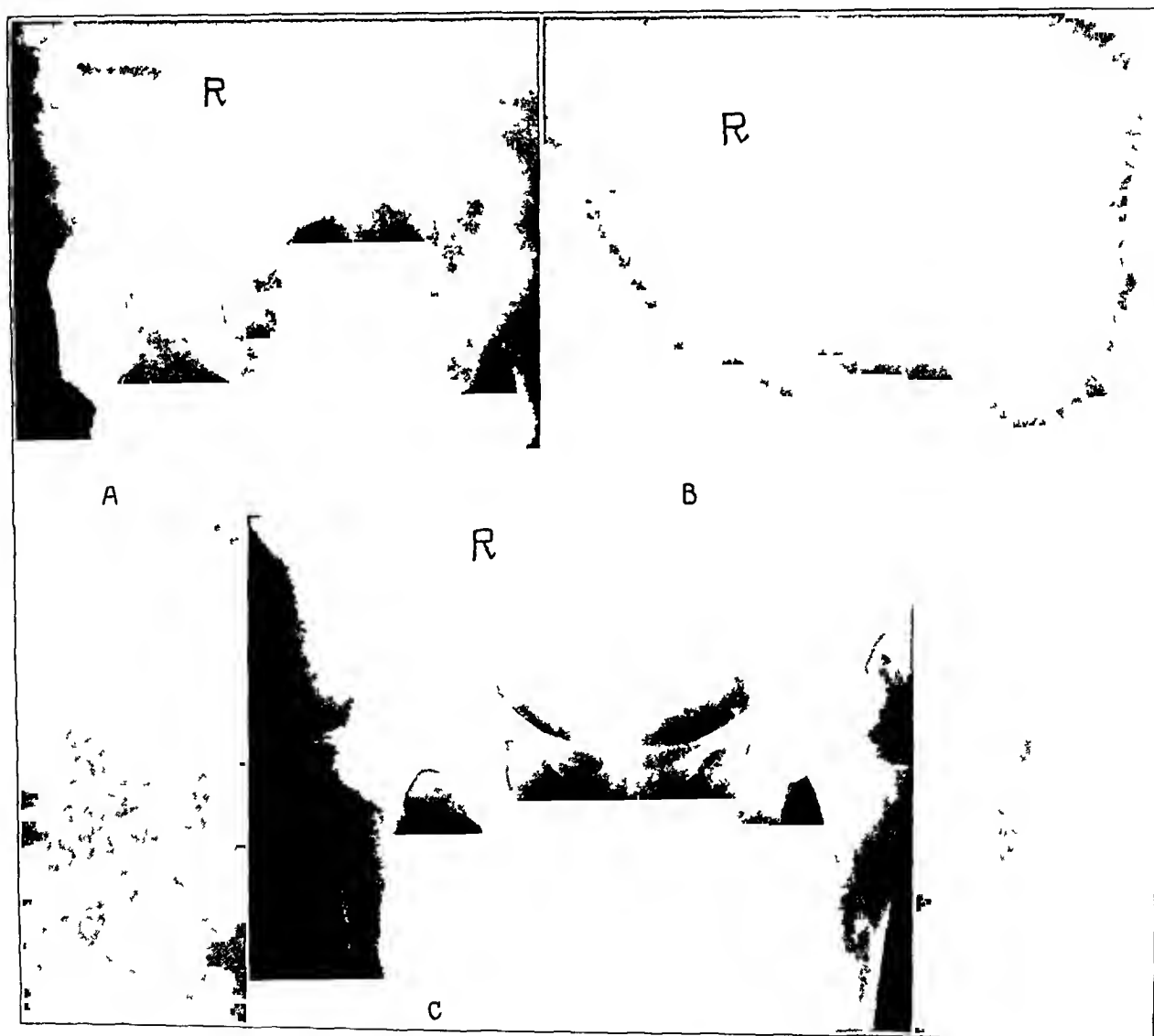


Fig 37 (case 13) —*A*, roentgenographic appearance of the right hip on the day of injury. *B*, roentgenogram taken three days after closed reduction of the fragments. *C*, roentgenographic appearance of the right hip three years after the injury, showing a living femoral head which revealed slightly reduced density.

she came to the clinic for examination. The hip disclosed a full range of motion. No tenderness or disability could be elicited. Roentgen examination at the time, sixteen months after the injury, revealed a healed intracapsular fracture of the neck of the left femur (fig 39). The femoral head showed normal shape and

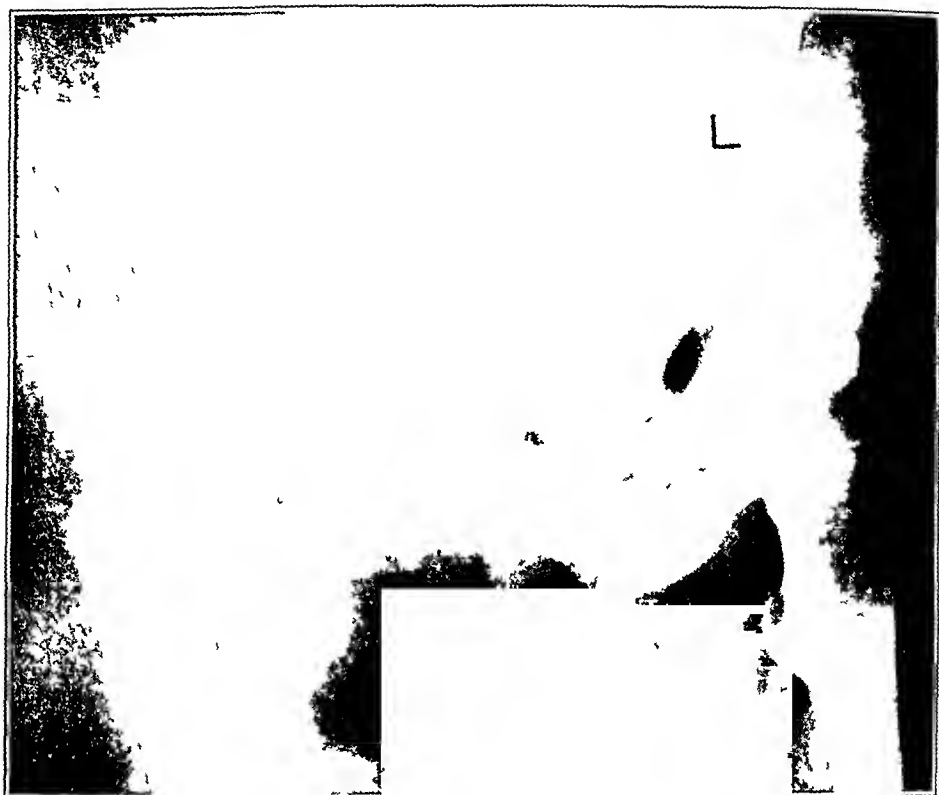


Fig 38 (case 14) —Roentgenogram taken two months after the injury, showing the healed intracapsular fracture of the neck of the left femur



Fig 39 (case 14) —Roentgenographic appearance of the left hip sixteen months after the injury. Note the healed fracture of the neck and the slight diffuse reduction in density of the head

appeared alive but slightly atrophic, as shown by its slight diffuse decrease in density. Two years and four months after the injury the patient reported that the hip was free from pain and functioned normally except for slight limitation of motion.

When nonunion has existed for some time before open reduction and reposition of the fragments is performed, bony union of the fracture, if the head is alive, may still result in spite of marked atrophy of the fragments. This is well illustrated by the case reported by Henderson,<sup>24</sup> which indicates that a prompt anatomic healing of the fracture notwithstanding the existence of nonunion of more than three years' duration may occur with a good functional result (fig 40). The marked diffuse

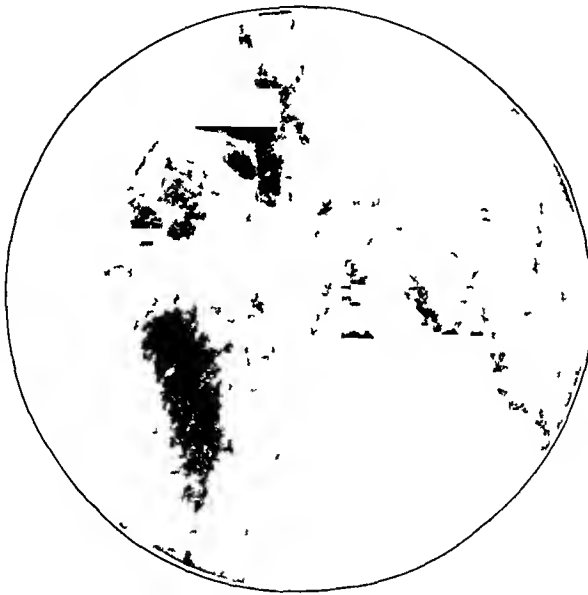


Fig 40—Successful bone graft for nonunion of more than three years' duration. Note partial restoration of the neck of the femur. The head is markedly atrophic with a small circumscribed area of reduced density about the fovea (after Henderson, *Ann Surg* 83:696, 1926).

decrease in density of the head, as in cases 6 and 7, is evidence that the head was probably alive and as such did not undergo secondary degenerative changes but atrophied from disuse.

#### COMMENT ON CASES IN WHICH HEAD SURVIVED AND FRAGMENTS UNITED

In the three cases of intracapsular fracture of the neck of the femur in which the roentgenogram indicated that there was survival of the head and in which there was either impaction of the fragments or early reduction and fixation of fragments, bony union took place. The head

<sup>24</sup> Henderson, M. S. Ununited Fracture of the Hip, *Ann Surg* 83:696, 1926.

retained its normal contour and its density varied with that of the surrounding bone showing reduced density from disuse at the end of the period of immobilization and a return to approximately a normal density after function was fully resumed. In case 12 coxa vara persisted, and new bony trabeculae were laid down across the head in the new lines of force. In cases 13 and 14 there was little change in the neck of the femur, and the head resumed almost normal appearance in roentgenograms.

The callus forms almost entirely in the intermediary zone, there being practically no new bone laid down on the surface of the neck. It appears to come from both fragments as is the case in the ordinary fracture. Bony union occurred in the one case of fracture with displacement of fragments following early reduction and fixation in abduction and internal rotation after the method of Whitman. However, there seems to be no good reason why nonunion should not occasionally result after good reduction and fixation of fracture of the neck with survival of the head as is the case with other fractures in various parts of the skeleton. In case of delayed or nonunion with survival and atrophy of the head of the femur it has been found that open operation with freshening of the fragments and fixation by a variety of procedures has been followed by bony union in a certain percentage of cases. This is exemplified in Henderson's case in which there was successful union after the use of a bone peg in a case of delayed union of three years' standing.

#### CAUSES OF NONUNION

There has been a great deal of controversy as to the causes of nonunion of fractures of the neck of the femur. They may be grouped broadly under four heads: (1) displacement of fragments, (2) excessive mobility of fragments, (3) necrosis of head of femur, (4) necrosis and erosion of neck fragments.

Exact reduction and fixation of fragments are undoubtedly the most important factors in obtaining bony union in case of intracapsular fractures of the neck of the femur as a group. This is shown by the variation in results that have been reported by different methods of treatment in which there have been variations in accuracy of reduction and degree and duration of fixation of fragments, also, by the great frequency with which bony union occurs in case of impacted fractures of the neck, when external fixation has been employed and sometimes when there has been no external fixation. It is generally conceded that the most efficient closed reduction and fixation of fragments is obtained by the Whitman abduction method of cast treatment. Portwich<sup>22</sup> reported thirty-one cases (67 per cent) of nonunion in fifty intracapsular fractures of the neck in which the Whitman abduction method was not used and only one case of nonunion among ten cases in which this method was used.

Campbell<sup>25</sup> treated twenty-nine fresh intracapsular fractures of the neck of the femur by the Whitman method, with bony union in twenty-four, nonunion in four, and in one the result was unknown. Of forty-four cases of ununited intracapsular fractures of the neck of the femur which came under his observation, Buck's extension was used in fourteen, plaster cast in nine, Hodgen's splint in four, sand bags in nine, osteopathy in two, ambulatory splint in one, and in five undiagnosed cases no treatment was given.

Necrosis of the head is undoubtedly an important cause of nonunion. When the circulation to the head is completely interrupted, the entire structure dies, and since the head and neck lie free in the joint there is no rapid attachment established with surrounding soft parts and consequently no survival of osteogenic elements along the fracture surface or periphery of the fragment-end such as occurs in a bone transplant located away from joints. Therefore, any callus that is formed for the repair of the fracture has to come from the distal fragment, and union between a completely necrotic and a living fragment is more difficult of accomplishment than between two living fragments. The slightest motion at the seat of fracture tends to break up the callus which has to bridge the defect and permeate, absorb and replace the dead bone. Of the fifteen cases here studied, there was complete necrosis of the head in nine and partial necrosis in one (case 7). Of these, there was nonunion in five cases, including the one case of partial necrosis, and bony union in the other five, including three cases in which nonoperative treatment was used, one case in which immediate beef bone pegging was performed, and one impacted case in which union was in the process of occurrence when death occurred on the twenty-fourth day. There was an impaction in two cases in which bony union was obtained, and in one case there was effective application of the Whitman abduction method of treatment. In one case of nonunion there was no treatment. In one case there was weight extension of the limb, and in two cases inefficient treatment was given with a plaster cast, as judged by the statement of the patient to the effect that the limb had not been fixed in marked abduction and internal rotation. The series is too small to judge of the exact frequency with which union takes place when the head is necrotic, but it would indicate that there is good opportunity for its occurrence in case there is impaction of fragments with external fixation or efficient reduction and fixation of fragments by the Whitman abduction method.

Erosion and absorption of the neck are factors that are secondary to the presence of nonunion and to movement of the fragments, whether the result of imperfect fixation or whether intentional after attempts at

<sup>25</sup> Campbell, W. C. Fractures of the Neck of the Femur, *Ann. Surg.* **70**: 600, 1919.



immobilization have been dispensed with Lang <sup>26</sup> thought that absorption of the neck is the primary cause of nonunion and sought explanation for it in the poor blood supply in the middle portion of the neck The bone which dies along the ends of the fragments, whether or not the head survives, is eventually absorbed and replaced by new bone as is the case with fractures in other locations There is no particular reason to assume that it is absorbed more extensively without replacement by new bone in a fracture in this region than in other regions In these cases there was about as frequent and as extensive erosion of the neck fragments in nonunion with survival of the head as in nonunion in the presence of necrosis of the head

#### ROENTGEN RECOGNITION OF NECROTIC AND LIVING HEADS

Since the state of nutrition of the head of the femur has direct bearing on the occurrence of nonunion and of disintegrative changes in it and on the type of treatment that should be carried out, it is of great importance to try to estimate this as nearly as possible by means of roentgenograms If the head remains alive, it will undergo the same degree of atrophy from loss of function produced by immobilization and of restitution produced by return of function as occurs in the neighboring bone of the ilium and distal fragment Consequently, the head and the distal fragment show about the same degree of reduction in density at the end of the period of immobilization, and reduced density persists throughout the period of disability In case of occurrence of bony union there is a gradual return to original density with the full resumption of function The arrangement of the newly deposited bone varies little from the normal except in case of union in coxa vara when shadows of heavy trabeculae will be seen along the new lines of force

In case of nonunion and marked functional disability, as in case 6, there is persistence of uniform reduction in density of the head When it becomes extreme as in cases of long standing, bony trabeculae may be entirely lost in relatively large areas of the head Evidences of collapse and disintegration of the weight bearing portion of the femur are not seen regardless of the degree of atrophy that may develop The shadows cast by the fragment of the neck in case of nonunion are gradually lost as erosion progresses

In case of necrosis of the proximal fragment there is a distinct difference in density between the shadow cast by the head and the neighboring living bone at the end of the period of immobilization treatment This difference is visible at the end of six weeks and is usually marked at the end of two and one-half or three months The head having lost its blood supply, has been unable to atrophy and casts a shadow of nor-

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<sup>26</sup> Lang A. Beitrage zur Lehre von den Schenkelhalsbrüchen auf Grund anatomischer und klinischer Studien, *Deutsche Ztschr f Chir* **135** 101, 1916

mal density while the neighboring living bone casts a shadow of reduced density as a result of atrophy of disuse. Subsequent changes in density in both head and neighboring bone vary according to whether or not bony union occurs and according to the use that is made of the limb. If there is nonunion, the neighboring living bone continues to cast a shadow of reduced density due to the protracted disuse. The necrotic head is more or less gradually invaded by blood vessels and connective tissue, but in the absence of functional stimulation there is very slow absorption of the dead bone with partial replacement by living bone. Consequently, it continues to cast a heavier shadow than the neighboring atrophic living bone for a prolonged period. In cases 2 and 3, the heads still cast uniformly dense shadows at the end of sixteen and thirteen months, respectively. The histologic evidences of absorption and beginning replacement by spongy bone and the roentgenologic evidence in cases 2 and 7 would indicate that a gradual irregular reduction in density in the ununited necrotic head is brought about in the course of years. Consequently, in cases of nonunion of long standing it should be difficult to distinguish between the cases in which the head remained alive and became atrophic, and those in which the head underwent necrosis with slowly progressive absorption and partial replacement by living bone. In general, the transformed necrotic head would be expected to cast a more blotchy and uneven shadow than the atrophied living head.

When there is necrosis of the head and bony union of the fracture occurs, the necrotic head casts a heavier shadow than the distal fragment at the end of the period of immobilization. With the resumption of function, the tissues of the distal fragment and in some instances of the round ligament are stimulated to invade the necrotic head with resultant absorption and replacement by new bone at a much more rapid pace than occurs when there is no functional stimulation as in the case of nonunion. This transformation is evidenced by an irregular reduction in density proceeding from the fracture line where the invasion is from the distal fragment and from the fovea where the invasion is from the round ligament. If the head is protected from too extensive weight bearing, its normal uniform density is gradually replaced by a more or less unevenly reduced density with little or no change in its contour. This is illustrated in cases 11 and 11 X. With the resumption of extensive weight bearing following this extensive replacement of necrotic bone by living bone, the head greatly increases in density but the outline of the new bone is irregular and blotchy, as shown in figure 35, case 11 X.

In case of necrosis of the head in which bony union occurs and there is too much weight bearing before invasion, and transformation of the necrotic bone has been brought about, the weight bearing portion of the head will show evidence of collapse in the roentgenogram with a depression of its articular surface and irregular dense shadows in the underlying bone due to compression of the broken-down necrotic trabeculae.

Invasion of the neck from the distal fragment results in irregular reduction in its density with abnormally arranged shadows of newly formed bone. In case 10, the greater part of the head had its density reduced as a result of rapid transformation during the eight and one-half months following the injury, and the nonweight bearing portion continued to cast a faint shadow during the subsequent three years due to the fact that motion in the hip was markedly limited and weight was not borne on it. Collapse and extensive irregular transformation in the weight bearing portion of the head of the femur after healing of the fracture of the neck is always indicative of necrosis of the proximal fragment. The condition is not one, as Axhausen thought, of arthritis deformans in the true meaning of the term.

#### BEARING OF OBSERVATIONS ON TREATMENT

The objective in the treatment of all fresh fractures of the neck of the femur, whether the head survives or becomes necrotic, should be to secure bony union with as nearly complete reduction of fragments as it is possible to obtain. This is best accomplished by means of the Whitman abduction and internal rotation method of cast treatment. The cast should be removed in from ten to twelve weeks, as this is usually adequate time, whether the head is dead or alive, for the occurrence of bony union although from four to six months may be necessary for it to become solid. From roentgenograms taken at the end of this time it should usually be possible to say whether the head survived or became necrotic, also, whether or not the fracture is united. When there is doubt about these points, a second or third roentgen examination after a few days or weeks will usually clear them up. When it is determined that the fracture is united and that the head remained alive, the patient should be allowed to go about on crutches, and in from one to two months begin weight bearing. Collapse of a surviving head from subsequent weight bearing has not been reported.

On the other hand, if it is found that the fracture is united and that the head became necrotic, the resumption of function should be very much more gradual than when the head survives. The patient should walk with crutches, and weight bearing should be delayed for several months, from six to twelve, in order to allow time for the invasion and replacement of the necrotic bone by living bone and to avoid possible collapse of the weight bearing portion and deformity of the head with a bad functional result. A necrotic head with bony union usually produces a more painful hip than a living head, and weight bearing cannot be tolerated for some time. Hence, collapse does not usually occur although the patient is privileged to walk on the limb. The progress of transformation in the head may be followed in the roentgenogram as

in case 10 and the appropriate time for discarding clutches judged accordingly. Movement of the limb without weight bearing should be encouraged, as functional stimulation hastens the rate of transformation of the head. If a patient is seen in whom slight or moderate collapse has occurred, weight bearing should be discontinued and an opportunity given for organization of the head. If the collapse and deformity are marked, there may be extensive disability resembling arthritis deformans, and a Whitman reconstruction operation with excision of the deformed head may be indicated.

If there is nonunion with survival of the head and the patient is a good operative risk, there is some question as to the best plan of treatment. In case the injury is not too old, the fragments of the neck not extensively eroded and good approximation of freshened fragments can be obtained, the bone pegging operation of Albee may be indicated. If the case is of several years standing or if the neck has been eroded, either the Whitman or the Brackett reconstruction operations should be performed. If the fracture is ununited and the head has undergone necrosis the best procedure, when the patient's symptoms and general condition warrant operation, would appear to be the Whitman reconstruction operation of excision of the head, insertion of the upper end of the shaft in the acetabulum with displacement of the trochanter downward and attachment to the side of the shaft. Either the bone pegging or the Brackett operation would be expected to result in a high percentage of nonunion, and even if union occurred, stiffness and a deformed head would be likely to give a poorer functional result than the Whitman operation. In the case of necrosis of the head of long standing with revascularization and partial or complete replacement by new bone, a Brackett or bone pegging operation would probably give a poor result here either from adhesions or from nonunion.

#### SUMMARY

The only source of blood supply to the head in case of complete intra-capsular fracture of the neck of the femur is the ligamentum teres and the extent of the vessels contained in it at the time of occurrence of the fracture determines its subsequent vitality. If the vessels are adequate the head remains alive, but if inadequate it undergoes necrosis. While the blood vessels are more abundant in younger persons, they may be adequate to keep the head alive after fracture in the aged. The necrosis involved the entire head in all of the cases in which it occurred except one. The relative frequency of living and necrotic heads after fracture of the neck cannot be judged from the fifteen cases here reported (six living and nine necrotic) since most of them were selected because of the fact that they afforded material for pathologic study or because of

the presence of special features, as nonunion, necrosis of the head with bony union, or survival of the head with bony union in the aged. However, it is evident that necrosis of the head is a not uncommon occurrence.

When the head remains alive, there may be either bony union or nonunion of the fracture. Bony union occurs in a large percentage of cases if the fracture is well reduced and immobilized by the Whitman abduction method or if it is put at rest in case of impaction. Nonunion is the usual result of faulty reduction and fixation although it may follow efficient reduction and fixation as is sometimes the case in fractures in other locations. When the head survives and union occurs, it undergoes atrophy of disuse during the period of immobilization and subsequent disability and regains its normal bony density with the restoration of function. It never collapses subsequently from weight bearing, but when there is nonunion the head usually remains permanently atrophic. The articular cartilage is thinned by absorption along its attachment to bone and may be partly replaced by bone-marrow and new bone.

In case of inadequate nutrition of the proximal fragment through the round ligament, the bone, bone-marrow and cartilage become necrotic. Bony union may follow in case of efficient reduction and immobilization or in case of impaction. In this event, the head is gradually invaded by tissue growing across the healing fracture from the distal fragment, and in some cases from the hypertrophied round ligament, the dead bone, bone-marrow and cartilage are absorbed and more or less completely replaced by irregularly distributed new bone, bone-marrow and fibrous tissue. The weight bearing portion of the head may collapse before the result, but the prolonged avoidance of weight bearing may prevent this occurrence and a good functional result may be obtained.

Necrosis of the head predisposes to nonunion. When the fracture, after a period of treatment, remains ununited, the head is denser and casts a heavier shadow in roentgenograms than the surrounding living bone which has undergone atrophy. The necrotic head may be gradually invaded by newly formed tissue from the round ligament and from adhesions which form between the capsule and the eroded fracture surface. This tissue gradually replaces the necrotic marrow and absorbs the dead articular cartilage. Replacement of the dead bone by living bone takes place at a very slow rate. Consequently, the head may remain denser than the neighboring atrophied bone for at least from one to two years as seen in cases 2 and 3. The absence of active functional stimulation explains the slow rate of transformation in the head as compared with that which is seen in case of necrosis of the head followed by bony union. In the absence of weight bearing there is no collapse of the head as shown by a roentgenogram, but compression of it between trochanter and

acetabulum may lead to some erosion of necrotic articular cartilage and breaking down of subcortical trabeculae as seen in case 3

It should usually be possible by means of roentgenograms to tell after from six to ten weeks have elapsed whether the head is dead or alive in the event of either union or nonunion. The living head undergoes more or less uniform atrophy of disuse and in case of return of function it maintains the original density for a long period of time. Its density dead tissue has been absorbed and replaced, giving a poor functional may eventually become uneven and blotchy as a result of invasion, absorption and replacement by new bone. Collapse and deformity developing after union has occurred is always indicative of necrosis of the head.

It would appear from these observations and from other published reports that all fresh fractures of the neck of the femur are best treated by Whitman's reduction and abduction cast fixation. If bony union follows with survival of the head, there is usually restoration of satisfactory function within a period of a few months. If bony union follows with necrosis of the head a painful hip may persist or may return after usage. Weight should not be borne on the head for many months in order to allow sufficient time for creeping substitution of the necrotic head by new bone and thereby prevent possible collapse and deformity of the head. If nonunion occurs and the head remains alive the choice of treatment in a patient who is a good operative risk lies between an autogenous bone peg and a Whitman or a Brackett reconstruction operation depending on the changes in each case. If the head is necrotic and nonunion results, a Whitman reconstruction operation should be performed.

#### CONCLUSIONS

- 1 After complete intracapsular fracture of the neck of the femur, the proximal fragment may either remain alive as a result of nourishment received through the vessels of the ligamentum teres or become necrotic.

- 2 If efficient reduction and fixation are carried out early and sufficiently long maintained, bony union follows in a high percentage of the cases in which the head remains alive and in a smaller but no inconsiderable percentage of cases in which the head becomes necrotic.

- 3 If bony union occurs in the presence of necrosis of the proximal fragment, the limb should be protected from weight bearing for many months while creeping substitution of dead head by new bone is taking place. If marked collapse and deformity of the necrotic head should develop, a Whitman reconstruction operation with excision of the head may sometimes be indicated.

4 If nonunion results and the head remains alive, a patient who is a good risk may be operated on by use of an autogenous bone peg or by the Whitman or the Blackett reconstruction method according to the case

5 In case of nonunion with necrosis of the head, there may be slow invasion of tissue from the round ligament or from adhesions with very gradual absorption and partial replacement of the necrotic tissue by living bony elements. However, the proper operative treatment in case of nonunion with necrosis of the proximal fragment appears to be excision of the head and the performance of a Whitman reconstruction operation

6 By roentgenographic studies, it is usually possible to differentiate between a head that remains alive and one that becomes necrotic because of their difference in density which develops during the period of disuse and because of their difference in internal structure and occasionally in contour which develops during the period of reconstruction

# A COMPARISON BETWEEN SIMULTANEOUS EQUAL-SIZED CLOSED OBSTRUCTIONS OF THE DUODENUM AND THE ILEUM\*

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In a previous study,<sup>1</sup> it was indicated that there were marked anatomic and physiologic differences between obstructed loops of the duodenum and of the ileum in the dog. The anatomic observations have been in a large measure corroborated by Dragstedt, Lang and Millet.<sup>2</sup> These investigators showed that distention of the intestine caused the greatest interference in the duodenum because of the anatomic distribution of the blood vessels in the duodenal wall.

We have nothing new to add to our anatomic studies already reported, but wish to record some additional data on the secretion rates, intra-intestinal pressures, distensibilities, and bursting pressures of equal-sized loops of the duodenum and ileum.

## EXPERIMENTAL WORK

Dogs were anesthetized with ether, and simultaneous closed loops of equal size were made in the terminal duodenum and in the terminal ileum. This procedure was carried out by finding the duodenojejunal ligament and tying a flat tape tightly across the lumen of the duodenum without damaging the blood supply in the mesentery. Ten centimeters were then measured up the duodenum, and a second tape was passed around the bowel and tied tightly. This made a closed loop of terminal duodenum from which gastric, pancreatic and biliary secretions were excluded. In the same way the 10 cm segment of terminal ileum was

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\* Submitted for publication, Feb 12, 1930

\* From the Department of Surgery, the University of Rochester School of Medicine and Dentistry

\* Aided by a grant from the Committee on Scientific Research of the American Medical Association

1 Morton, J J. The Differences Between High and Low Intestinal Obstruction in the Dog. An Anatomic and Physiologic Explanation, Arch Surg **18** 1119 (April) 1929

2 Dragstedt, C A, Lang, V F, and Millet, R F. The Relative Effects of Distention on Different Portions of the Intestine, Arch Surg **18** 2257 (June) 1929



measured off from the ileocecal junction and occluded (fig 1) The animals were anesthetized every twenty-four hours, and the contents of the closed loops were aspirated with a needle and syringe After the contents were measured carefully, they were returned to the loop from which they had been withdrawn In this way it was hoped to get an accurate measure of the secretion rate without disturbing the abnormal intra-intestinal pressure relations which had occurred Eight animals were

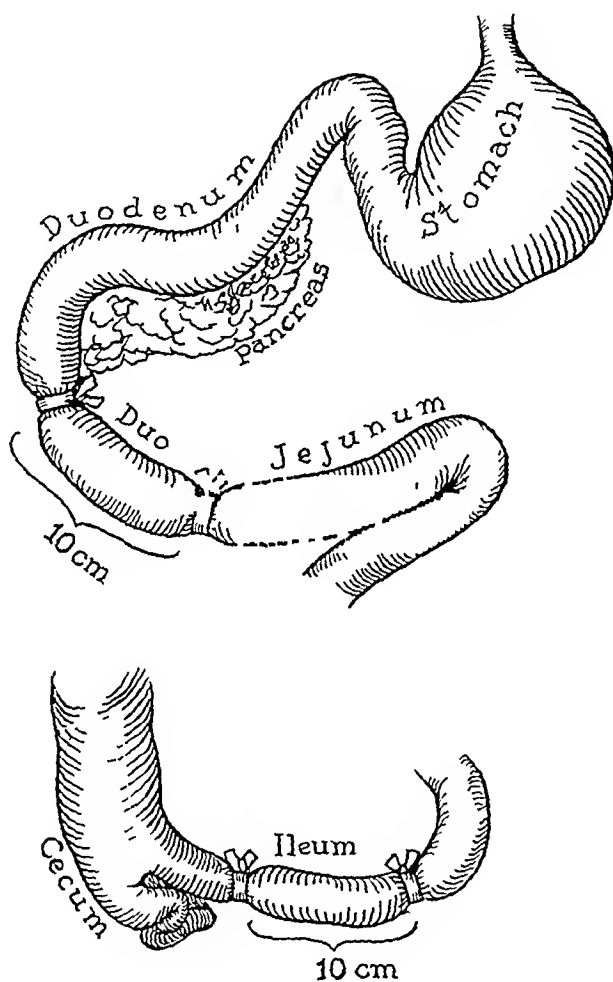


Fig 1—Diagram showing closed loops of equal size which were made in the terminal duodenum and terminal ileum

used for this part of the experiment, and the results are recorded in in table 1

There is a striking difference in the amount of secretion which accumulates in the closed duodenal and in the ileal loops The secretory rate for the ileum is practically negligible, the amount even after seventy-two hours being only approximately 1 cc In the duodenum, on the contrary, there is a rapid production of fluid so that the average reading for the eight animals at twenty-four hours was 11.3 cc The secretion mounts sharply in the second twenty-four hours, averaging

35.7 cc for seven animals at the end of forty-eight hours. During the third day following, the pressure becomes so great as to rupture the duodenal loop at the occluding tape or through the puncture holes. We do not believe that the measured quantities obtained at seventy-two hours represent the actual amount secreted in spite of the fairly high figures, because a majority of the animals already show leakage at this

TABLE 1—*Amount of Secretion in Closed High and Low Loops in Cubic Centimeters Compared with Toxicity as Measured by Blood Chemistry in Milligrams per Hundred Cubic Centimeters*

Dog Number		Time of Operation	24 Hours	48 Hours	72 Hours	Observations at Autopsy
27-288	Duodenum	0	5	20		Died 60 hours after operation, small leak in duodenum, ileum intact, 2.5 cc found
	Ileum	0	0.5	2.5		
	Nonprotein nitrogen	26	97	320		
	Chloride	490				
28-110	Duodenum	0	10	40	60	Died 72 hours after operation, rupture duodenum, general peritonitis, ileum intact
	Ileum	0	1	1	1	
	Nonprotein nitrogen	27.5	35.3	89	158	
	Chloride	515	465	418	380	
28-131	Duodenum	0	2.5	35		Died 60 hours after operation, leak in duodenum, ileum intact, general peritonitis
	Ileum	0	0.2	0.5		
	Nonprotein nitrogen	28	30.8	38.7		
	Chloride	490	430	369		
28-92	Duodenum	0	3	20		Died 50 hours after operation, leak in duodenum, general peritonitis
	Ileum	0	0	2		
	Nonprotein nitrogen	25	31	72		
	Chloride	490	450	279		
28-148	Duodenum	0	5		30	Died 90 hours after operation, leak in duodenum, ileum intact, general peritonitis
	Ileum	0	0.5		2	
	Nonprotein nitrogen					
	Chloride					
28-161	Duodenum	0	42	70	75	Leaked at puncture hole, free fluid, fresh peritonitis, died 72 hours after operation, very large dog
	Ileum	0	0	0.5	0.5	
	Nonprotein nitrogen	31	40	66	133	
	Chloride	480	465	390	330	
28-210	Duodenum	0	15	50	60	Localized peritonitis, free fluid, fresh general peritonitis, died 72 hours after operation, large dog
	Ileum	0	0.5	0.5	0.5	
	Nonprotein nitrogen	33	30	80	120	
	Chloride	440	390	445	350	
29-220	Duodenum	0	8	15	20	Localized peritonitis, leak at puncture hole, fresh fluid, died 72 hours after operation
	Ileum	0	0	0.5	0.5	
	Nonprotein nitrogen	36	37	48	90	
	Chloride	490	465	355	320	
Average figures for the series { Duodenum		0	11.3	35.7	49	
{ Ileum		0	0.33	1.07	0.9	

time. A comparison of the secretion rates in the duodenum and ileum can be easier appreciated by observing figure 2, which is a graph of the average figures for the series. This study also brings out the essential differences in function between the duodenum and the ileum. Physiologists have long taught that absorption occurs in the ileum and that the most active secretion takes place high in the small intestine. It would appear from these experiments that this is true, and that the current is toward the lumen of the bowel in the duodenum and away from it in the ileum.

The average length of life for twelve animals with this type of double closed loop obstruction was approximately seventy-one hours.

It is interesting to note that the animal which lived the longest of the group—ninety hours—had a low secretion in the duodenal loop, only 30 cc being present at seventy-two hours. Another animal, which died eighty hours after operation, had only 20 cc of fluid in the duodenum at seventy-two hours. These figures are well below the average for forty-eight hours. Without exception death was due to peritonitis and the leak occurred in the duodenal segment. It is probable that the high obstruction is alone responsible for the outcome in these animals. If it were not for the rupture and peritonitis, the animals might survive for a much longer period. This observation lends support to the contention of Chenut,<sup>3</sup> who claimed that the toxic products are absorbed

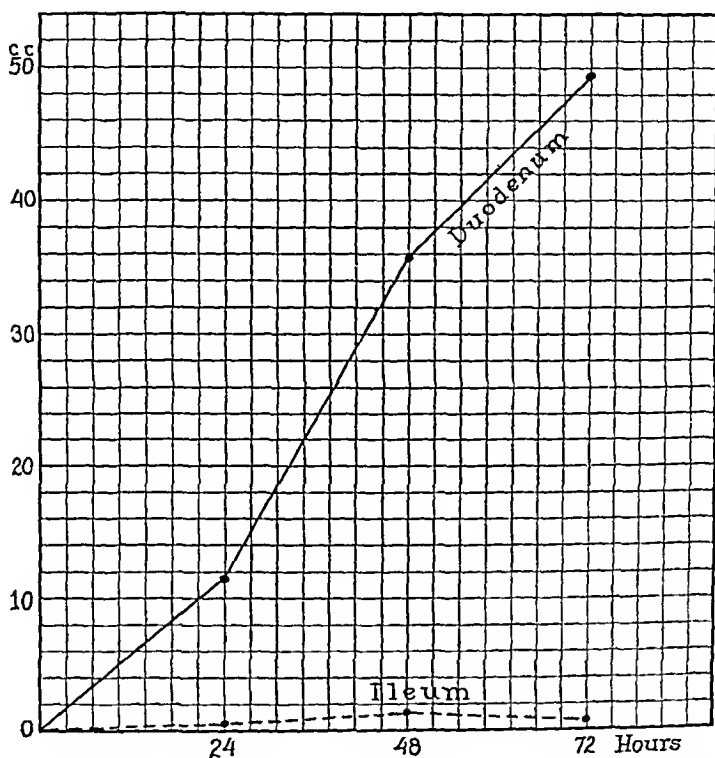


Fig 2—A comparison of the secretion rates of equal-sized closed segments of duodenum and ileum

through the peritoneum, and that absorption is practically nil when the obstructed loops are put in an extraperitoneal position. It also raises the question whether any toxin is ever absorbed through the intact wall of the bowel.

Six animals were used for a study of the intra-enteric pressures developed in these closed segments. A water manometer, as originally described by Owings, McIntosh, Stone and Weinberg<sup>4</sup> was used. The

3 Chenut, A. L'expérimentation dans l'occlusion mécanique de jeuno-ileon, *Rev de chir* 64 474, 1926

4 Owings, J. C., McIntosh, C. A., Stone, H. B., and Weinberg, I. A. Intra-Intestinal Pressure in Obstruction, *Arch Surg* 17 507 (Aug) 1928

measurements show a great variation depending on the state of the intestine at the time. The peristaltic waves cause decided increases in pressure and it is difficult to judge the exact end point for any reading. In general, the sustained pressures in the duodenum were slightly higher than in the ileum just after operation. Within the first twenty-four hours the pressure sustained and peristaltic mounted steadily in the duodenal segment until it was from four to seven times as great as in the ileum. There was a slow rise also in the pressure within the ileum. In the second twenty-four hours the pressures in the duodenum were not so striking. We feel that technical difficulties with the apparatus failed to bring out the differences that must have been present. We consider that the readings for the first twenty-four hours were an index

TABLE 2—*Difference in Intra-Intestinal Pressure Measured in Millimeters of Water in Obstructed Closed High and Low Loops*

Dog Num- ber	Opera- tion	4 Hrs	8 Hrs	12 Hrs	16 Hrs	20 Hrs	24 Hrs	48 Hrs	72 Hrs	Cause of Death
27-217	Duodenum	100-120	110-140	240-310			210-520			Died suddenly 24
	Ileum	5	5	20			80			hours peritonitis
28-180	Duodenum	55					280-350	120-170		Dog chloroformed
	Ileum	50					50	60		localized peritonitis
28-207	Duodenum	30	30	70	100	130-160	250-370	200-300	180-250	Localized peritonitis and early diffuse peritonitis
	Ileum	20	20	20	20	20	40	170	270	
28-219	Duodenum	40	50	90			150-400	160-230		Diffuse peritonitis died 52 hours
	Ileum	20	20	20			50	70		
28-284	Duodenum	20	20	20-30	50	100	100	150	70 80	Died 80 hours
	Ileum	20	20	20	30	30	40	100	140	localized and diffuse peritonitis
28-148	Duodenum	20-30					40-100		160 200	Died 80 hours gen
	Ileum	10					10		50	eral peritonitis

of the real differential pressures in the two loops but our later readings do not indicate the true state of affairs. In several of our animals there was an early leakage of material around the stem of the duodenal cannula, and perhaps this accounts for the poor results. Possibly the caliber of the manometer was too gross to register the values accurately. The results of these pressure measurements are given in table 2. Photographs of manometer pressure records are also shown (fig. 3).

A great many measurements were made to test the amount of distensibility in length and circumference of segments of the duodenum and the ileum. These observations were taken while finding the amount of air pressure necessary to determine the bursting pressures of the segments. Table 3 shows the observations on the segments tested immediately and one, two, four and twenty-four hours after death.

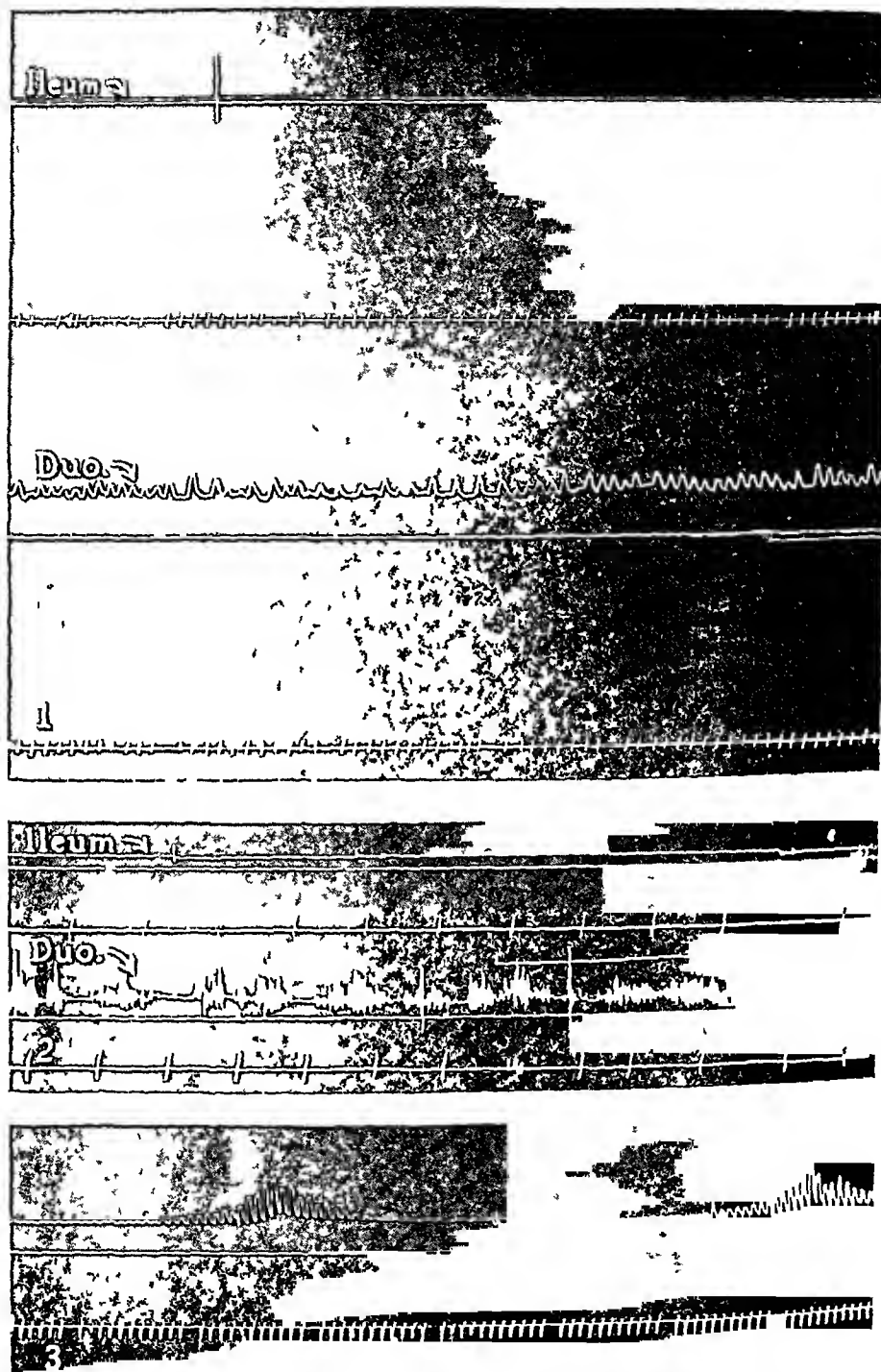


Fig 3—Illustrations showing (1) obstructed loops of duodenum and ileum at twenty-eight hours, time interval, five seconds. The ileum is inert, but the duodenum has continuous peristalsis at a fairly high pressure, (2) obstructed loops of duodenum and ileum at forty-eight hours, time interval, one minute, (3) obstructed duodenum at twenty-four hours, time interval, five seconds. The peristaltic waves are well shown in addition to the substained pressure above the base line

Practically all the tests made were similar to these readings. The immediate samples indicate the wide range of variation in distensibility in length and width, and the great amount of elasticity of the segments. A pressure over 1,000 mm of mercury was necessary before rupture occurred. The ileum seemed to possess a greater lengthening power than the duodenum, but the distention in circumference was about equal. The powerful duodenal musculature made the duodenal segments able to withstand a somewhat greater pressure. In even as short a period as one hour after death the elasticity of the segments seemed to be altered. The stiffening due to rigor was best demonstrated by the burst-

TABLE 3—*Segments Immediately, One, Two, Four and Twenty-Four Hours After Death*

Dog Num- ber	Segment	Length in Cm		Circumference in Cm		Pres sure Mm Mer cury	Point Rupture	
		Nor- mal	Com plete Dis- tention	Nor- mal	Com plete Dis- tention			
23-98	Duodenum	65	120	50	75	1500	Antimesenteric small hole	
	Immediately after death	Ileum	90	230	40	70	1200	Blew end off
			99	210	40	55	1050	Blew end off
6	Duodenum	70	95	40	75	1400	Antimesenteric wide hole	
	Immediately after death	Ileum	100	120	30	65	1080	Antimesenteric small hole
			90	115	30	50	1175	Antimesenteric small hole
7	Duodenum	100	140	50	80	725	Antimesenteric	
	Dead 1 hour	Ileum	100	175	35	70	800	Antimesenteric
			100	1775	35	75	790	Antimesenteric
4	Duodenum	105	130	43	95	800	Antimesenteric end blew off	
	Dead 2 hours	Ileum	110	130	22	75	500	Wide hole mesentery
			100	130	23	60	680	Wide hole mesentery
3	Duodenum	100	130	50	90	990	Antimesenteric	
	Dead 4 hours	Ileum	100	160	40	85	770	Wide hole antimesenteric
			100	160	40	95	760	Wide hole antimesenteric
5	Duodenum	100	110	35	75	830	Blew end off antimesenteric	
	Dead 24 hours	Ileum	100	105	30	575	700	Blew end off
			110	120	30	50	690	Blew end off

ing pressures, the average of the readings being only about 750 mm of mercury, as against nearly double the figure for the specimens tested immediately.

The results of this study confirm our previous observations on the physiologic differences between the high and the low obstructions in the dog. The most striking phenomenon is the rapidly increasing secretion in the duodenal segment in contrast to the comparatively inert secretion in the segment of the ileum. The increase in fluid content is naturally accompanied by a raised intra-enteric pressure which is well demonstrated at the end of the first day after operation. This

increase in pressure within the upper segments is apparent in the following days as well, but in these experiments technical difficulties, leakage, etc., masked the undoubtedly much greater hydrostatic pressures in the duodenum. Rupture always occurred in the duodenal segment, and death was invariably due to peritonitis. Studies are at present in progress to test further the physiologic differences in high and low intestinal obstructions.

# FORTY-SECOND REPORT OF PROGRESS IN ORTHOPEDIC SURGERY ~

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## CONGENITAL DEFORMITIES

*Torticollis*—Howell<sup>1</sup> operated on twenty patients by means of a subcutaneous tenotomy of the sternal head of the sternomastoid muscle, with nineteen complete cures. He used a plaster of paris cast for four weeks, this was then bivalved and retained for another four weeks. Treatment by a masseuse completed the cure in from three to six months.

[ED NOTE—The tenotomy of the sternal portion alone seems to us inadequate in many cases. The simplicity of the open operation hardly warrants the risk entailed in a subcutaneous operation.]

*Congenital Dislocation of the Hip*—Fairbank<sup>2</sup> chose congenital dislocation of the hip as the subject for the Lady Jones lecture at Liverpool in 1929. The first half of the lecture he devoted to pathologic anatomy,

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\* This Report of Progress is based on a review of 226 articles selected from 638 titles dealing with orthopedic surgery appearing in the medical literature between Nov 30, 1929 and May 1 1930. Only those papers which seem to represent progress have been selected for note and comment.

1 Howell, B W. Brit M J 2 714 (Oct 19) 1929

2 Fairbank H A T. Brit J Surg 17 380 1930



basing his remarks on experience in fifty open operations on the hip joint and on a study of thirty-six specimens, many of which repose in Dupuytren's Museum in Paris and are beautifully reproduced in the paper

The anatomic changes in the pelvis, bones, ligaments and muscles were reviewed in detail. Fairbank left his readers to draw their own inferences from this mass of pathologic anatomy. It would seem that the prime cause of the dislocation was the poor development of the upper rim of the acetabulum, and that this factor was further responsible for the prolonged immobilization required after reduction. The difficulties of reduction were due (1) to diminution in the size of the acetabulum, which after a few years became triangular because of the unresisted overgrowth of the anterosuperior and posterior margins, and (2) to a narrowing of the capsule between the true and false acetabulum socket. This isthmus owed its origin to factors both outside and inside the capsule. The narrowing within the capsule was caused by a horizontal fold of a synovial membrane situated at the level of the true acetabulum. This fold was flattened out when the head of the femur rode up on the ilium and folded up into a band when the head was pulled down toward the true acetabulum, thus impeding its progress. The narrowing without the capsule was caused by the constriction of the iliopsoas tendon, which became more taut when the head of the femur was pulled down and so offered an obstruction to reduction. These facts pointed to the choice of the Denuce method of reduction in preference to the Lorenz method. In addition to the diminution in the size of the acetabulum and to the presence of the isthmus, a third difficulty of reduction existed, namely, the shortening of the adductor muscles, which it was necessary to stretch or rupture prior to reduction.

In the second half of the lecture Fairbank discussed the causation of the limp, the reason for pain in unreduced dislocations, and treatment. He considered that the limp, though made worse by the shortening of the limb, was due (1) to diminution in the power of abductors because of the restriction of the area of the ilium from which the muscles could arise, (2) to diminution in the leverage of the abductor muscles owing to the position of the head of the femur, (3) to the relative weakness of the abductors because of the simultaneous powerful contraction of the adductors in their endeavor to transmit the weight of the body from the pelvis to the leg and (4) to the instability of the fulcrum which allowed the head of the femur to ride up and down and backward and forward on the ilium.

The aim of treatment, according to Fairbank, was twofold—to provide a stable joint and to prevent subsequent arthritis. Reduction at an early age alone would ensure this double success. In the older patient

stability might be achieved by reduction, but it was unlikely that arthritis would be avoided, for this reason Fairbank did not attempt to reduce a bilateral dislocation in patients more than 6 years of age, or a unilateral dislocation in patients over 9

Fairbank resorted to open reduction only after closed reduction had failed, if he had to operate whether reduction was successful or not he always made a new roof by turning down a bone shelf. In his belief, antetorsion sufficient to demand osteotomy or to cause a redislocation was rare. He considered failure of the upper lip of the acetabulum to grow out a more potent factor leading to redislocation and when the hip redislocated in spite of efficient after-fixation he advocated making a new shelf. He did not approve of transposition in irreducible cases, a procedure that he found difficult to use and one that was frequently followed by relapse. For the irreducible case in which increasing disability and pain developed in adolescent or adult life he advocated arthrodesis of the hip on the affected side in unilateral cases and on the worse side in bilateral cases, but he warned against fusing the joint in too much abduction. Osteotomy might be of value in a few selected cases in which the pain was due not to arthritis of the joint but to strain on ligaments and muscle weakness. He had no experience with the shelf operation advocated by Dickson and Allison, nor did he like excision of the head for old unreduced dislocations.

[ED NOTE—The editors regard this general discussion as excellent in its general exposition of the question. They would be more inclined to favor the shelf operation in the irreducible cases in preference to arthrodesis.]

Mandruzzatto<sup>3</sup> reporting the statistics on treatment for congenital dislocation of the hip at the Instituto Orthopedico Rizzoli from 1899 to 1927, stated that he found 3 685 dislocations in 2 578 patients. Of these patients, 85.02 per cent were females and 14.58 per cent males. There were 42.94 per cent bilateral and 57.06 per cent unilateral dislocations. Of the latter group 39.02 per cent were on the right side and 21.83 per cent on the left. In females bilateral dislocation was found in 36.96 per cent on the right side in 29.82 per cent and on the left in 17.72 per cent. In males bilateral dislocation was found in 5.97 per cent on the right side in 5.39 per cent and on the left in 4.11 per cent.

[ED NOTE—The percentages are of total cases in males and females.]

Information in regard to heredity and familial tendency was obtained in 2,276 of the 2,578 cases. Direct heredity was found in 6.54 per cent and was slightly greater on the male side. A familial tendency was found in 16.69 per cent of the cases and was definitely more marked on

<sup>3</sup> Mandruzzatto. *Chir. d. org. di movimento* 14:200, 1929.

the male side. There was nothing to indicate that delivery had any definite rôle in the etiology. Concomitant deformities occurred in 3.04 per cent of the cases.

In the 2,578 cases diagnosis was made during the following age periods: before 1 year in 2.32 per cent, from 1 to 3 years in 47.36 per cent, from 3 to 6, in 29.36 per cent, from 6 to 10, in 9.65 per cent, from 10 to 15, in 5.77 per cent, and after 15 years in 5.54 per cent. The statistics showed that diagnosis is constantly being made at an earlier age.

The treatment was bloodless reduction by the Paci-Lorenz method in 88.48 per cent of the cases. Open reduction was performed in 3.16 per cent and some form of reconstruction in 3.08 per cent. The statistics further showed that there was a regional distribution of the cases.

[ED. NOTE—These statistics from such an important clinic in the treatment for this particular condition are significant. We regret that they do not include a study of the end-results as well.]

Pitzen<sup>4</sup> described a method of traction that had been used in Lange's Clinic in cases of dislocation of the hip. A dressing of zinc oxide glue was applied to the leg and covered with a plaster of paris cast. Then traction was applied up to 12 Kg. in an abducted position, which was gradually increased. As soon as the trochanter was pulled down to the height of the acetabulum the abduction was increased 120 degrees. With that method, Pitzen had been able to reduce severe dislocations with a high-standing head in patients up to the age of 8 years.

#### NUTRITIONAL DISTURBANCES OF THE BONE

*Osteitis Fibrosa Cystica*—Hannon, Shorr, McClellan and Dubois,<sup>5</sup> Bauer, Albright and Aub,<sup>6</sup> and McClellan and Hannon<sup>7</sup> reported studies made in sequence in a case of osteitis fibrosa cystica. Studies were made particularly of the calcium and phosphorus metabolism. The calcium excretion remained constant at a fairly high level. A positive calcium balance with a high calcium intake was secured. The calcium metabolism was almost identical with that of a patient receiving daily 100 units of parathyroid extract-Collip. Two parathyroids were removed, the study of which revealed no abnormality. The calcium metabolism was unaffected by their removal. With a diet rich in

4 Pitzen. *Ztschr. f. orth. Chir.* 52:529, 1929.

5 Hannon, R. R., Shorr, E., McClellan, W. S., and Dubois, E. F. *J. Clin. Investigation* 8:215, 1930.

6 Bauer, W., Albright, F., and Aub, J. C. *J. Clin. Investigation* 8:222, 1930.

7 McClellan, W. S., and Hannon, R. R. *J. Clin. Investigation* 8:249, 1931.

calcium and with the addition of calcium lactate, roentgenograms showed a progressive increased density of bone and a decrease in the size of a cyst in the femur. Changes in phosphorus intake, which theoretically should affect the calcium, had no effect on calcium retention. Pituitary extract produced a marked increase in fecal calcium elimination, while thyroid extract increased the excretion of calcium in both urine and feces.

*Spotted Bones*—Newcomet<sup>8</sup> described a single case of "spotted bones" or osteopoecilia which occurred in an Irishman aged 50. It was discovered accidentally when one hand was subjected to roentgen examination for a supposed fracture. The lesions were generalized in cancellous bone and were symptomless. The etiology was unknown and the prognosis good.

#### TUBERCULOSIS

*Tuberculosis of the Hip*—Roederer<sup>9</sup> observed five patients with juxta-articular tuberculosis developing in the rim of the acetabulum and giving rise to disease of the hip. The process developed slowly, and it was a long time before symptoms appeared in the hip. This corresponded to the period of extra-articular osteitis. The diagnosis during this period was difficult. The roentgenogram often was not clear, particularly when the lesion was situated on the anterior or posterior lip of the acetabulum. Once the symptoms of arthritis had set in, the evolution was rapid.

Sorrel,<sup>10</sup> in a summary of his report to the thirty-eighth Congress français de chirurgie (1929), discussed the indications and the results of fusion operations in Pott's disease. Two reasons made it difficult to appraise exactly the value of operations. The disease was greatly variable, as to both severity and type. In children, healing took place often with complete cicatrization of the lesion and bony fusion. In the adult complete healing seldom took place. It was necessary to observe a large series of patients for a long time. A small series might give an entirely erroneous idea. The second reason was that it was not known exactly how to produce osteosynthesis. Was its action that of a splint to the spine alone or to the spine and the entire lesion? Did it modify the vascular supply? Was it simply palliative or really curative?

Sorrel advocated no operation in children. In adults the operation was advisable, but it was difficult to decide on the time. In some instances the diagnosis could not definitely be made. In others it was

8 Newcomet W S. Am J Roentgenol 22 460 1929

9 Roederer C. Presse med 37 1925 1929

10 Sorrel E. J de chir 34 439 1929

difficult to determine if the lesion was inactive or healing under orthopedic measures. At all events, the operation should be performed at the period of least virulence. He used both the rigid graft of Albee and the flexible graft of Dujainier or Delangière. For cervical Pott's disease, he advocated a plaster bed, in others, a hard bed in the prone position for six months, and then a corset of plaster or celluloid for a year.

In 106 patients during ten years he had 60 excellent results, 21 good results, 9 neither good nor bad, and 16 bad. He noted that it was difficult to value the operation alone because of the associated general and orthopedic care.

#### INFANTILE PARALYSIS

*Polomyelitis Antistreptococcus Serum*—Rosenow<sup>11</sup> said that a streptococcus having peculiar neurotrophic and immunologic properties on isolation had again been cultivated from the throat, brain and cord, and for the first time in pure culture from the spinal fluid in cases of typical poliomyelitis occurring in another epidemic. It had been demonstrated consistently in smears of the spinal fluid in twenty-three patients and in each of twelve monkeys that had typical poliomyelitis following inoculation of virus. It was proved to be absent in the spinal fluid before the virus was injected.

The results from the use of poliomyelitis antistreptococcus serum were observed in the treatment of an additional series of patients with epidemic poliomyelitis and of monkeys with experimental poliomyelitis, in neutralization of virus in vitro, and in immunization of monkeys with the streptococcus against poliomyelitis virus.

The curative action of the serum in the treatment in this new series, as in several previous series of cases of poliomyelitis, seemed unmistakable and was manifested in one or more of several ways. Annoying symptoms, such as headache, pain, hyperesthesia, fever and a high pulse rate, often disappeared promptly. Paralysis seemed to be prevented if the serum was given in the preparalytic stage before there was marked evidence of involvement of the spinal cord. Progressive paralysis was seemingly arrested in many cases, including those with beginning bulbar symptoms, and the death rate and incidence of residual paralysis were markedly lowered.

The results obtained from serum treatment were in accord with those reported previously by Rosenow, Rowan, Sugg, Clarke and Dow, and Dively. The results from the use of the poliomyelitis antistrepto

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11 Rosenow, E. C. *Poliomyelitis Streptococcus Serum*, J. A. M. A. 94:777 (March 15) 1930.

coccus serum compared favorably with those reported by Aycock and Luther, from the use of convalescent serum. The total mortality rate (10 per cent) in this series of patients, as in those reported previously, was far lower, especially when the serum was given in the early stages of the disease (in which the mortality rate was 4 per cent), than in the control cases occurring in the same epidemic (33 per cent), and was far lower than that which usually occurred in this disease (25 per cent of 224 cases occurring in Minnesota in 1928).

Since the results from the use of this serum in the prevention and treatment of experimental poliomyelitis in monkeys were in agreement with the striking beneficial action again noted in clinical cases, it was concluded that poliomyelitis antistreptococcus serum, when properly prepared, had curative power in poliomyelitis. Its further trial, especially in the concentrated form in which serum reactions were largely eliminated, was indicated.

*Epidemic of Poliomyelitis*—Lomer and Shirref<sup>12</sup> gave a résumé of the poliomyelitis epidemic in Ottawa in 1929. Of 181 patients suspected of having the disease, the diagnosis was established in 141, and these persons were treated, 109 patients recovered completely, 29 recovered with paralysis, 2 died with paralysis and 1 died without paralysis. Convalescent serum was given intramuscularly to all 115 patients admitted without paralysis, 109 of these patients recovered completely, 5 recovered with partial paralysis and 1 died without paralysis.

*Experimental Poliomyelitis*—From a careful study of the epidemiology of poliomyelitis, Aycock<sup>13</sup> postulated a constant virus reservoir in a community through which the disease was disseminated by direct contact. In this way about one person in fifty was exposed each year, the exposure in most cases producing subclinical immunization. The disease occurred in children because they were the nonimmunized persons in the community. He expressed his belief that the cause of seasonal variation in a number of patients was not crowding of the schools, but a seasonal change in individual resistance. He felt that one can in no way control the virus, and that one's efforts should be directed toward raising individual resistance in the prevention and control of this disease.

*Intradermal Immunization of Monkeys with One Set of Injections of Poliomyelitis Virus*—Rhoads<sup>14</sup> attempted to immunize four monkeys against poliomyelitis by one intradermal injection of poliomyelitis virus.

12 Lomer, T. A., and Shirref, W. T. *Canad. M. A. J.* **22**, 228, 1930.

13 Aycock, W. L. *Am. J. Pub. Health* **20**, 41, 1930.

14 Rhoads, C. P. *J. Exper. Med.* **51**, 1, 1930.

He gave multiple injections intradermally of 16 cc of a 5 per cent saline suspension of the glycerolated spinal cord of a monkey infected with pooled, mixed poliomyelitis virus. In none of the monkeys were there any symptoms of poliomyelitis. One month later the monkeys were bled and neutralization tests were carried out. Active immunity was produced in each of the four monkeys.

[ED. NOTE—Aycock's explanation is interesting and seems plausible. Rhoads' experiment in immunizing monkeys may be a stepping stone toward immunization of human beings. We doubt the willingness of anyone at present to be immunized with living virus.]

#### PYOGENIC INFECTION

*Osteochondritis of the Symphysis Pubis*—Pierson<sup>15</sup> reported four cases of nontuberculous osteochondritis of the symphysis pubis. Two cases followed suprapubic prostatectomy, infection presumably occurred at the time of operation or subsequently due to erosion from the closely apposed drainage tubes. One of these patients died of general sepsis. A third case occurred without apparent cause and was cleared up by drainage. The culture showed *Staphylococcus aureus*. The final case developed after a septic hemiotomy. Pierson expressed his belief that this condition was probably more common than is usually supposed, as Beer had seen one case each year for the past twelve years. All the cases followed suprapubic prostatectomy, and recovery took place without drainage. The symptoms usually were tenderness over the symphysis pubis, pain down the legs and exaggeration of symptoms on motion. The roentgenograms helped relatively little as there is a wide variation in the roentgenograms of the normal pubic symphysis.

*Juxta-Articular Osteitis*—From a study of 168 cases of juxta-articular osteitis of various types, Andrieu<sup>16</sup> concluded: 1. There are cases of osteitis in which the evolution, the diagnosis and the prognosis are profoundly modified by the fact that the condition is close to a joint. 2. These cases occur in persons of all ages, but are more common in infancy and particularly in early infancy. 3. The symptoms are not clearcut. The symptoms arising from the reaction in the adjacent joint are the most important. 4. In the presence of signs of chronic arthritis following successive abscesses, after having eliminated the various causes of articular inflammation, one need not make a diagnosis of rheumatism, one should always think of the possibility of a juxta-

15 Pierson, E. L. *Surg. Gynec. Obst.* 49:834, 1929.

16 Andrieu, M. *Rev. d'orthop.* 16:522, 1929.

articular osteitis 5 The duration of the evolution can be extremely long 6 The immediate prognosis depends on the menace of the osteitis to the neighboring joint 7 The treatment must be directed toward preservation of the articulation 8 In osteitis of the hips one must choose cases in which surgical approach seems easy, otherwise treatment should be conservative 9 When either conservative or operative treatment is used, the joint must be immobilized until all symptoms have disappeared

#### NEOPLASMS

*Changes in Primary and Metastatic Tumors of the Bone Following Various Doses of Roentgen Rays*—Herendeen<sup>17</sup> said that the response of primary tumors of the bone or the changes induced by the application of a known amount of roentgen or radium rays could be predicted with a fair degree of accuracy provided that certain other information was available First of all, one should know the age of the patient, equally important was detailed knowledge of the character of the tumor in a given case By character was meant the degree of malignancy rate of growth, size, location, origin and tendency to produce or destroy bone

In the order of sensitivity to irradiation, primary tumors of the bone might be classified as follows (1) endothelial myeloma or Ewing's tumor, (2) giant cell tumor, (3) multiple myeloma, (4) osteogenic sarcoma of the destructive type, (5) osteogenic sarcoma of the mixed or destructive and productive type and (6) osteogenic sarcoma of the sclerosing, bone-producing type

Herendeen warned against the use of heavy dosage in the treatment for giant cell tumors Not only might heavy doses be followed by severe, unnecessary reactions or pathologic fractures, but more important, bone regeneration was likely to be retarded

From the data accumulated to date, Herendeen concluded that roentgen treatment of giant cell tumors had passed the experimental stage and that with few exceptions the results from every angle were far superior to those secured by surgical measures

*Ewing's Sarcoma Small Round Cell Sarcoma of the Bone*—Copeland, Geschickter and Bloodgood<sup>18</sup> studied sixty cases of Ewing's sarcoma They found that it comprised 15 per cent of 400 cases of sarcoma of the bone It was predominantly a disease of early life, 95 per cent of the patients were less than 25 years of age There was a definite

17 Herendeen, R E Radiology **13** 326, 1929

18 Copeland, M M, Geschickter, C F, and Bloodgood, J C Ewing's Sarcoma, Small Round Cell Sarcoma of Bone, Arch Surg **20** 246 (Feb) 1930



history of trauma in 22 cases. Intermittent pain, increasing in severity and frequency, was the predominant symptom. A tumor, either small or involving the whole bone, was palpable in 90 per cent of the cases. The long bones were most frequently involved. Pathologic fractures were rare. Fever was observed with the metastases and often in the early stages with growth of the tumor. Bence-Jones bodies were never found in the urine. Except for occasional secondary anemia, nothing unusual was found in the blood. Roentgenograms showed a diffuse lesion near the midshaft. Increased density of bone with a widened cortex was the commonest observation. There was slight periosteal reaction with occasional osteophytes parallel to the cortex. Tumors in the soft parts were usually encapsulated by a thin fibrous tissue. The microscopic features were found to be the best criteria for diagnosis. The tumor consisted of small polyhedral cells in compact areas with round or oval nuclei and with scanty cytoplasm. Necrosis of cells was observed in areas a little removed from the blood vessels. In all cases in which metastases occurred (43 cases) the patients died. The commonest site for metastases was the lung, the skull, spine and scapula were next in frequency. The patients studied had lived from twenty months to nine years after the onset of symptoms, 8 of them being alive and apparently well. In most of the cases the first diagnosis had been inflammatory disease of the bone, a condition which the early roentgen appearance closely simulated. The treatment found to be best was, in the lower extremity, amputation below the upper third of the femur, followed by irradiation, in the upper extremity, resection followed by irradiation. From this study the authors could not determine the origin or histogenesis of the tumor.

*Chondrosarcoma of the Bone*—Phemister<sup>19</sup> objected to the inclusion of chondrosarcoma under the heading of osteogenic sarcoma, as had been done in the present Registry of Bone Tumors. Of sixty-one cases of sarcoma of the bone studied he found ten which showed largely cartilaginous cells that could be designated as chondrosarcoma. Such tumors cast characteristic, blotchy, irregular shadows in the roentgenogram. Although they grew rapidly, they usually gave rise to metastases much later and consequently the prognosis was better. They might arise either centrally or peripherally in the ends of the bone shafts and might invade the veins, creating thrombus formation.

[ED. NOTE.—Copeland et al. have summarized in admirable fashion their observations in this peculiar condition. Their work should be a

guide to any one who studies Ewing's tumors. The articles by Herendeen and Phemister are also enlightening, and make us feel that real progress is being made in the knowledge of tumors of the bone.]

#### ARTHRITIS

*Calcium Metabolism in Arthritis*—Copp<sup>20</sup> made an intensive study of the calcium metabolism in one case of atrophic arthritis and in one case of hypertrophic arthritis. He found a retention of calcium in hypertrophic arthritis and a loss of calcium in atrophic arthritis. In general, he found that all acids increased the excretion of calcium. With sodium bicarbonate there was also an increased excretion of calcium. Phosphoric acid caused better retention of calcium than any other drugs administered. This acid was given in the dilute form, 20 drops before meals.

*Results of Blood Culture in Acute Polyarthritis*—Jordan and Boland<sup>21</sup> studied the bacteriology of the blood in thirty-two cases of acute arthritis with multiple involvement of the joints. As controls they made blood cultures on sixteen patients in the same hospital who were suffering from various diseases, but with no involvement of the joints. In the cases of arthritis the diagnosis was acute rheumatic fever or subacute articular rheumatism. Of the sixty-seven blood cultures made in cases of arthritis, thirty-seven remained sterile for one month or longer, thirteen showed contaminations and sixteen showed organisms: a gram-negative short bacillus and a few plates on subculture, and a gram-positive club-shaped bacillus. No arthritis was produced in rabbits by the intravenous inoculation of these organisms. Of the twenty-three cultures made in control cases, sixteen remained sterile and seven showed contaminations.

[ED. NOTE—The results of these authors seem as inconclusive as those of the many other workers who have attempted to study the bacteriologic aspects of arthritis. It seems impossible to isolate a specific organism at present, but it is hoped that some progress will eventually result from the vast amount of data being accumulated.]

*Sympathetic Gangliouectomy*—Adson and Rowntree<sup>22</sup> have applied sympathectomy (lumbar and cervicodorsal) to cases of chronic polyarthritis. Patients were selected in whom the disease had not progressed

20 Copp E. F. F. Calcium Metabolism in Arthritis. *Arch. Int. Med.* **45** 136 (Jan.) 1930.

21 Jordan E. P., and Boland I. P. *J. Infect. Dis.* **46** 148 1930.

22 Adson A. W. and Rowntree L. G. *Surg. Gynec. Obst.* **50** 204 1930.

fat enough to cause destruction of the points and in whom all known foci of infection had been removed. The authors also drew attention to the vasospastic syndrome which had been temporarily relieved by baking diathermy and vaccines. The presence of the vasospastic syndrome was determined in each case by Brown's "fever test" in which, after the injection of foreign protein, simultaneous readings of the temperatures of the mouth and skin were made. Sympathectomy had not been applied to arthritis of gonorrheal origin.

Six cases were carefully reported. In these sympathectomy had been done on either the lumbar or the cervicodorsal sympathetic chain or both, depending on the extremities involved. Unless the arthritic destruction of the joint was too advanced to permit a return of function, the patients without exception improved. They gained weight, and the motion of the joint improved. The moisture, coldness and feeling of heaviness of the extremity diminished and the muscle power increased.

*Parathyroidectomy in Ankylosing Polyarthritis*—Oppel<sup>23</sup> stated that his investigations and also those of three other Russian observers showed that a majority of the patients suffering with atrophic, ankylosing arthritis had a high calcium level in the blood and a decrease in the electro-excitation of the muscle. These conditions, he observed, were the opposite of those found in tetany. He therefore reasoned that parathyroidectomy might be indicated in such cases. Samarin found improvement in 33 per cent of forty-nine patients following the removal of two parathyroids. Oppel expressed his belief that such an operation primarily destroyed the hypercalcemia, stopped the progress of ankylosis and beneficially influenced the function of voluntary muscles.

[ED. NOTE—This work seems highly experimental, and careful data are not presented to convince us that parathyroidectomy is justified in chronic arthritis.]

*The Large Bowel in Chronic Arthritis*—Fletcher and Graham<sup>24</sup> made a roentgen examination of the large bowel in sixty patients with chronic arthritis. In 65 per cent of these patients they observed changes that they considered abnormal. There were changes in tone, haustral markings and length. Atony was sometimes seen in the whole colon, though usually in the cecum where it might be extreme. These abnormalities were markedly improved by dietetic treatment with coincident improvement in the arthritis.

23 Oppel, W. A. *Ann Surg* 90:978, 1929.

24 Fletcher, A. A., and Graham, D. *Am J M Sc* 179:91, 1930.

*The Colon in Relation to Chronic Arthritis*—Fishbaugh<sup>25</sup> emphasized the importance of eliminating the colon as a focus of infection in the patient with chronic arthritis. He had followed a series of sixty female and fourteen male patients, in whom, after all other foci had been eliminated, the colon was found to be the disturbing factor. The various etiologic factors were chronic constipation, chronic or subacute colitis, bands or adhesions, diverticula, rectal cyst or hemorrhoids. Roentgen examination of the colon for four or more successive days was of great aid in determining the diagnosis of sluggish colon. Except in cases requiring surgical measures, treatment consisted of a bulky diet, mild laxatives, and irrigations with a cecal tube. After irrigations an active culture of acidophilus was left in the cecum. Eight cases were not followed, of the remaining seventy-two, forty-two were quiescent, twenty-two showed improvement and eight no improvement after treatment.

*Spondylitis Deformans*—Shanz<sup>26</sup> noted that the bony proliferations in spondylitis were more pronounced on the right side than on the left. He felt that on the left the aorta acted as a support to the spine. He thought that this same factor was involved in scoliosis in which the dorsal curve was toward the right in the majority of cases.

#### CIRCULATORY DISTURBANCES

*Volkmann's Ischemic Paralysis*—Meyerding<sup>27</sup> reported on 128 cases of Volkmann's ischemic paralysis observed at the Mayo Clinic, in 36 of these operation was performed. The average age of the patients was 24 years and the average duration of the contracture, three years. The results were most encouraging in young patients with recent injury. The patients in group 1, with deformity of several days' or weeks' duration, whose hands showed the typical clawlike contracture, but whose arteries pulsated well and whose hands were warm, practically all responded to treatment with the Jones extension splint. Group 2 consisted of those who had deformity of several months' duration with cold hands and diminished pulsation, but whose fingers could still be brought out straight. These patients responded less favorably to the Jones method of treatment; yet one hesitated to operate until the treatment by gradual extension had been given a fair trial. Group 3 consisted of patients who were older and in whom the contracture was of

25 Fishbaugh, E. C. *Am J Surg* 7:561, 1929.

26 Shanz, A. *Ztschr f orth Chir* 53:42, 1930.

27 Meyerding, H. W. *Volkmann's Ischemic Contracture* J. A. M. A. 94:394 (Feb 8) 1930.

longer duration. These patients had marked deformity and atrophy, and because of contracture of the capsules the fingers and wrists could not be straightened easily, even with force. The pulsation was impaired and the muscles were ropelike on the flexor side. There were scars from sloughing with impairment of motion at the elbow and of supination. These patients demanded surgical procedures. Definite benefit could always be expected as far as correction of the deformity was concerned, but the loss of function in the muscles and the subsequent changes in the bones produced partial impairment of the extremity. There was little to be gained by the treatment of patients in group 4, although the deformity might be corrected by tenotomy and osteotomy, little function resulted and the impairment in circulation and the involvement of nerves sometimes necessitated amputation. A combination of gradual preoperative and postoperative extension with lengthening of the tendon and neurolysis followed by physiotherapy was often indicated.

*Peripheral Vascular Diseases*—Adson and Brown<sup>28</sup> said that sympathetic ganglionectomy and trunk resection was a surgical procedure of considerable magnitude which one was justified in using in the treatment of patients with advanced Raynaud's disease, in the early developing vasospastic cases of scleroderma, in cases of thrombo-angitis obliterans and in other cases in which vasospasm of the collateral arteries existed. The operation was probably indicated in other and borderline cases, but should be employed with caution, for the procedure was not a cure-all for all peripheral vascular diseases. The authors had operated on six patients with Raynaud's disease of the feet. In every case complete and permanent relief had been obtained. Four patients with scleroderma had been operated on. In early cases in which the scleroderma was less marked, the results had been excellent and a conservative estimate was from 70 to 80 per cent relief. They believed that more effective treatment of patients with scleroderma depended largely on early diagnosis and the institution of therapeutic surgical measures before fibrosis and atrophy had taken place. Operations had been performed on twenty patients with thrombo-angitis obliterans of the lower extremity. Four of these had been failures in that amputation had had to be performed in from two weeks to a year after operation. In sixteen patients the surface temperature had increased, but not to the degree observed in Raynaud's disease. The increase in the elimination of

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<sup>28</sup> Adson, A. W., and Brown, G. E. Thoracic and Lumbar Sympathetic Ganglionectomy in Peripheral Vascular Diseases, *J. A. M. A.* 94:250 (Jan. 25) 1930.

heat, relief of pain and healing of ulcers had frequently been spectacular. In four cases thoracic sympathetic ganglionectomy had been performed for thrombo-angitis obliterans affecting the hands. The results had been eminently satisfactory. The authors said that about one of every six or seven cases observed in the last two years had fulfilled requirements as far as the indications believed necessary for the operation were concerned.

#### DISEASES OF THE NERVOUS SYSTEM

*Sympathectomy*—Leriche and Fontaine<sup>29</sup> studied (1) the cicatrization of sympathetic trunks which had been sectioned and (2) the pathologic rôle of neuromas of sympathetic cicatrization. On the basis of two observations, they believed that the cicatrization might explain the recurrence of symptoms after a period of amelioration. The symptoms might be topographically different, but of the same general type as the original trouble. Such cicatrices might greatly diminish the therapeutic value of sympathectomies.

*Periodic Paralysis*—Yoshimura<sup>30</sup> observed that periodic paralysis of the extremities was often concurrent with diabetes or with glycosuria. Examination of blood drawn during an attack of paralysis showed that the magnesium content was far in excess of the calcium content. It is known that magnesium has a paralyzing effect on the neuromuscular apparatus. In experiments on animals the author observed that either the administration of the magnesium or the intravenous injection of dextrose led to typical paralysis of the extremities. In a patient to whom dextrose was administered during an attack of paralysis of the extremities the paralytic symptoms became more severe. After the injection of calcium, however, the paralysis subsided. On the basis of these observations the author concluded that the etiologic factor in periodic paralysis of the extremities was a shifting of the calcium-magnesium equilibrium of the blood serum.

*Myeloradiculitis*—Strauss and Rabiner<sup>31</sup> reported seven cases of acute invasion of the nerve roots and spinal cord for which they had coined the name myeloradiculitis. In all cases there had been a rapid onset after slight malaise and with infection of the upper respiratory tract in most cases. The symptoms had been radiating pain, occasionally with areas of hypo-esthesia or hyperesthesia, and weakness of the

29 Leriche, R., and Fontaine, R. *J de chir* **34** 439, 1929.

30 Yoshimura, K. *Munchen med Wchnschr* **76** 1921, 1929.

31 Strauss, I., and Rabiner, A. M. *Myeloradiculitis*, *Arch Neurol & Psychiat* **23** 240 (Feb.) 1930.

extremities with flaccid paralysis in three cases. In several instances there had been transient disturbance of sphincter control. In all there had occurred rapid and practically complete recovery in from eighteen hours to two months. Intravenous typhoid therapy had been used, but recovery had been so rapid that its value in this condition could not be estimated.

[ED. NOTE.—The similarity between the cases reported and others that we have seen diagnosed poliomyelitis is striking. Further information will be required to give a clearer understanding of the difference, if any exists.]

*(To be continued)*

## THE OPERATIVE TREATMENT OF LESIONS OF THE LOWER EXTREMITIES IN DIABETES MELLITUS\*

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AND

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The present report is based on 281 operations performed on the lower extremities of patients with diabetes mellitus and covers a seven year period ending Dec. 31, 1929. See figure 1. In order to standardize as many factors as possible patients operated on by other members of the staff and a large number treated without operation have not been included.

### TREATMENT OF THE PATIENT

Medically these patients have been taken care of by Dr. E. P. Joslin and his associates Drs. H. F. Root, P. White and W. Curtis, or by Dr. F. G. Brigham, his associate Dr. W. Stevens and his former associate Dr. R. R. Wheeler. The patients have remained throughout, under the direct care of the internist who has assumed responsibility for all medical problems that arise. It has been his privilege to question the surgical progress of the patient if response to diabetic treatment was other than that expected, a persistent high level of the blood sugar or an unusual resistance to insulin frequently being the first sign of sepsis in an amputation stump or of undrained pus in a foot. It has been his duty to make operation as safe as possible at any time it was indicated and, subsequently to safeguard the patient from coma or hypoglycemia.

A patient entering the hospital with a lesion of the foot is seen by the surgeon some time on the day of admission and within a few hours if extensive infection is present. Once the surgeon has seen the lesion, the entire responsibility for its treatment is his. With few exceptions, the time of operation is determined by the condition of the foot rather than by the condition of the patient and rests therefore with the surgeon. In general, operation is done as soon after admission as a definite decision is reached as to the type of operation indicated, sometimes within a few hours, usually within twenty-four. The surgeon, too, must decide on the type of operation to be performed and if it is amputation, the level at which it should be done. It would be an unwise surgeon, however, who did not freely utilize the store of information his medical confiere

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Submitted for publication, March 1, 1930.

\* From the New England Deaconess Hospital.



has available relative to many factors that influence the operative procedure

#### CLASSIFICATION OF CASES

In the treatment, as well as in the discussion, of so-called "diabetic gangrene," a definite understanding of the type of lesion under consideration is essential. Our experience has been entirely in accord with that of Collier and Marsh<sup>1</sup> who in 1925 stressed the importance of proper classification. It has been our custom to consider a given lesion as due

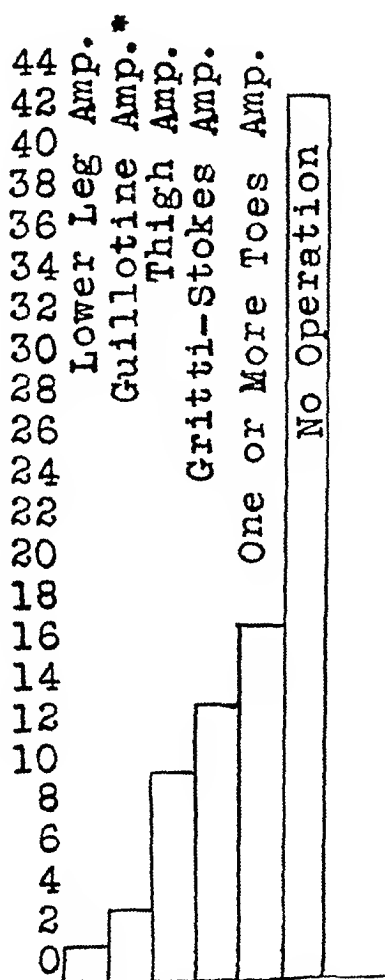


Fig 1—A diagram representing the disposition of eighty-four cases of lesions of the lower extremities during the year 1929

\*In these three cases, reamputation was done, they are therefore counted again under 'thigh amputations' (2) and 'Gritti-Stokes amputations' (1)

primarily either to infection or to arterial insufficiency with or without infection. In the former instance the blood supply may be abnormal, even to the absence of pulsation in the peripheral vessels but in such cases the collateral circulation has been developed to such a point that the foot is warm and essentially normal in appearance

<sup>1</sup> Collier, F. A. and Marsh, P. L. Lesions of the Extremities Associated with Diabetes Mellitus, J. A. M. A. 85:168 (July 18) 1925

## METHODS OF EXAMINATION

Almost without exception, decisions are based on clinical observations. We know of no suitable laboratory tests for the determination of the viability of a given foot under the existing conditions. In preparation for the examination the legs of the patient from mid thigh down are exposed to room temperature for at least five minutes. The most important points in estimating the circulatory background of a foot are

*Pain*—A history of pain on walking referred either to the calf of the leg or to the plantar surface of the foot suggests failing circulation. If after several months of such pain the patient becomes comfortable he may be considered to have developed a good collateral circulation. Severe pain at rest that is out of proportion to the infection present indicates a well developed arterial insufficiency and is a bad prognostic symptom.

*Appearance*—The more normal the appearance of the foot, the better is the circulation. The foot is examined in the horizontal, elevated and dependent positions. In a foot with failing circulation the skin is frequently smooth, thin and parchment-like, and the normal contour of foot and toes is gone. Such a foot on elevation quickly assumes a cadaveric pallor which disappears very slowly when the foot is horizontal, when the foot is dependent it becomes dusky or red and shiny, with tense, distended superficial veins.

*Temperature*—Temperature changes are elicited by palpation with either the back or the palm of the hand. Beginning above the knee a comparison is made between different levels of the same leg and similar levels of both legs. A foot that under room conditions is cold to the touch has a bad circulatory background. A sudden change of temperature at some point in the leg denotes, as a rule, absence of much collateral arterial development. In general changes in temperature conform with changes in color and are most marked with the foot dependent.

*Palpation of Peripheral Vessels*—The most important single blood vessel is the dorsalis pedis artery. Normally, pulsation can usually be felt. Buerger<sup>2</sup> found it in all but one of two hundred apparently normal feet. We consider the presence of good pulsation in this artery to be one of the most important observations. Any local operative procedure undertaken in its absence must be done only after careful consideration.

## CONDITIONS DUE PRIMARILY TO INFECTION

In the group of conditions due primarily to infection fall our most important cases. Here, carefully selected and properly done operations followed by painstaking after-care have frequently resulted in saving

<sup>2</sup> Buerger. *Circulatory Diseases of the Extremities*, Philadelphia, W. B. Saunders Company, 1924, p. 132.

useful feet Proper prophylaxis would have prevented operation One or more of the following observations are common to this group 1 Pulsation of the dorsalis pedis artery is usually present 2 The foot is warm and of good color It may be definitely cooler to touch than the knee, but there is no definite level at which the change is obvious 3 Osteomyelitis without gangrene is common 4 Pain is only in proportion to infection and usually less than that from a similar lesion on the foot of a patient without diabetes Not infrequently there is little or no pain, and the affected part is almost anesthetic 5 Gangrene is found only in the presence of severe infection or after trauma

Local operations in this group are frequently successful and usually safe

#### CONDITIONS DUE PRIMARILY TO ARTERIAL INSUFFICIENCY

Extremities in which there is an insufficiency of arterial circulation are characterized by the following observations 1 No pulsation is present in the peripheral blood vessels including at times the femoral at the groin 2 The foot is cold, blanches on elevation and becomes dusky or red and shiny when dependent Between the midfoot and the knee, there is frequently a definite level at which the temperature changes 3 Osteomyelitis with gangrene is common 4 Pain is nearly always out of proportion to the local lesion 5 Gangrene is common

Local operations in this group are rarely successful and frequently are dangerous Infection plus a painful, pulseless foot is the beginning of most cases of septicemia

#### NATURE OF INFECTION

It is impossible by clinical appearances to determine the character of the organism at fault Some of the feet, the type so frequently referred to as showing "bad streptococcus infections," have proved in cultures to be infected with *Staphylococcus aureus* or *albus* For the diabetic patient, the most important single organism is probably *Staphylococcus albus* Not only may it be the cause of a fatal septicemia, but its universal presence in the skin makes it the most common organism locally It is likely that the lowered resistance of the diabetic patient permits an organism ordinarily considered more or less nonpathogenic to become of clinical importance We have seen two cases recently in which it was recovered from the local lesion and repeatedly in pure culture from the blood stream One of these (fatal) was seen at another hospital The patient had a virulent infection, with gangrene, in spite of good arterial pulsation In our patient, the organisms were also obtained in pure culture from a section of an artery and a vein removed from the leg at the time of a guillotine amputation This patient confirmed the static-



gas bacillus infection in gangrenous feet Linton<sup>5</sup> described six cases appearing in stumps following amputations for gangrene at the Massachusetts General Hospital Greene<sup>6</sup> recently reported a similar complication In our cases, we had one such complication, although the organisms were discovered several times in amputated specimens The manner in which these infections develop is uncertain Tanner was of the belief that infection of an amputation stump occurs from the presence of organisms in the blood vessels Linton found organisms (*B welchii*) in one of the thrombosed vessels in an amputated leg although the possibility that these were outside rather than inside the vessels was not excluded Greene was unable to recover any organisms of this group from the amputated leg, although they were readily recovered from the patient before death It has been our policy to assume that such infections are contaminations from the skin introduced at the time of operation, unless there was a demonstrable gas bacillus infection before operation For this reason, we prefer no preoperative scrub with soap and water to one carelessly done and carried too close to the gangrenous area (See "Preparation of Patient" in later paragraphs)

The production of gas by the ordinary pyogenic organisms is a disturbing complication It is not uncommon to have gas escape on pressure around an open lesion Actual crepitus is rare, although in case 51185 it was present in the stump of an amputation through the lower part of the thigh, an extensive infection of the fascia lata having developed, extending from the end of the stump to the groin (fig 3) There was gas to the groin and the fascia was necrotic but the muscles were normal in appearance throughout Repeated attempts at cultivation, including that of the muscle tissue, showed only *Staphylococcus albus* Autopsy showed multiple sepsis but no evidence of *B welchii*

#### PRINCIPLES OF TREATMENT

The operative possibilities of a given leg can be determined by examination of the extremity The procedure indicated for a given patient can be determined only by a careful estimate of the patient as a whole What a waste of effort to do a lower leg or Gritti-Stokes amputation on one who, because of cerebral hemorrhage or failing eyesight, will be unable to use an artificial appliance!

Septicemia must be considered a possibility in every patient with diabetes and an infected foot The poorer the circulation the more difficult it is to localize infections Repeated chills and a temperature out of proportion to the local sepsis especially in a gangrenous foot without

5 Linton, R R Latent Gas Bacillus Infection Complicating Gangrene of Lower Extremity, J A M A **95** 183 (July 19) 1930

6 Greene P F Personal communication to the authors

a local abscess but with lymphangitis, usually mean septicemia. A normal temperature at admission must not be construed as evidence against such a diagnosis, for within a few hours it may reach 102 or 103 F.

#### TREATMENT FOR INFECTIONS

Surgical solution of chlorinated soda (Dakin's solution) has proved the most satisfactory local medication in cases with infection or slough. The wounds are kept constantly wet. Normal skin is carefully pro-

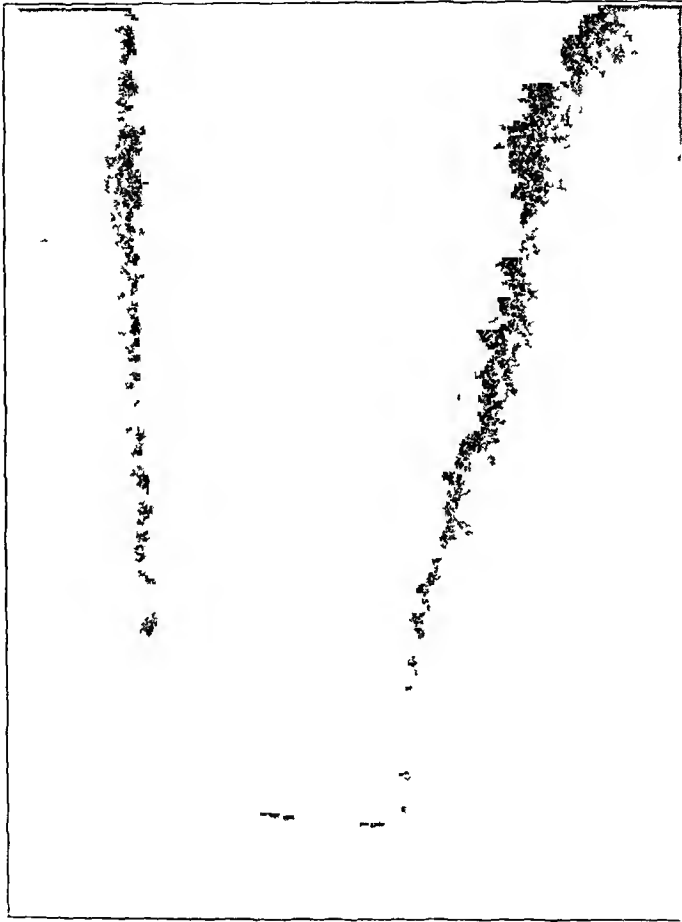


Fig. 3 (case 51185) —Roentgenogram of stump from which only *Staphylococcus albus* could be grown, showing gas to the upper third of the thigh. There was crepitus to the groin. The muscle was normal in appearance. All of the fascia lata was necrotic. No evidence of *Bacillus welchii* was found at autopsy.

tected. Once the gross infection is cleaned up, a change in the type of dressing is frequently indicated, tincture of myrrh (in water 1:24), dichloramine T (from 2 to 4 per cent) in chlorinated paraffin oil and balsam of Peru have all proved helpful. The improvement of the skin following daily applications of ultraviolet rays locally seems to indicate the usefulness of these rays in the treatment for local superficial infec-

tions Hexylresorcinol solution S T 37 (Sharpe & Dohme, in water 1 : 3) is nonirritating to normal skin, and has been used to advantage in such lesions as osteomyelitis of a phalanx of a toe which was being prepared for operation. We have found it of no value in the separation of a slough.

#### STIMULATION OF CIRCULATION

We have discontinued the use of external heat in all forms save the electric pad. The electric heater, hot water bags and hot and cold baths, when their application is left to the discretion of diabetic patients, are dangerous and ought not to be used. The feet of a diabetic patient may blister without discomfort to the patient. One of our most intelligent patients, who had taken alternating hot and cold baths for years, recently so burned one of his pulseless feet that he narrowly escaped amputation. We have seen innumerable toes taking months to heal after having been blistered by hot water bags.

The hyperemic exercises of Buerger have proved of most value. We are not prepared to explain the beneficial results to be derived from these exercises. Relief of pain in cases responding favorably is usually too early to be explained entirely on the basis of new collateral blood vessels. One gets more the impression of a readjustment of circulation to meet less diastolic demands, much like the response of the heart with anginal pain to a proper relation between rest and suitable exercise. Suffice it to say that we have seen patients unable to sleep because of pain in a foot or toe who with no treatment, except rest in bed, local applications to the open lesion (if present) and Buerger exercises, become perfectly comfortable within two weeks' time and keep free from pain when up and around through carefully graded active exercise, in addition to the continuation of the passive exercises to be described later. One needs the conviction of its merits to be able to impress the average patient with the value of a procedure that seems so simple. Our routine is (1) lying in bed with the feet elevated about 60 degrees for two minutes, (2) sitting up with the feet dependent for three minutes, and (3) assuming a horizontal position with an electric pad applied to the foot and lower part of the leg for five minutes, a total of ten minutes to the cycle, which is repeated, if the condition of the patient permits six times each period. Hospital patients have three and in some cases four periods a day. When the pain is severe, the cycle has to be modified to suit the individual patient. Orthopedic exercises of the type ordinarily used to strengthen the muscles of the foot and limber up the toes are done when the feet are in the dependent position.

Once free from pain, the patient must be careful when again becoming active. It is our policy to start the patient walking one-half minute

out of each hour, this period is increased by one-half daily as conditions permit, and the feet are kept elevated between walks

#### INDICATIONS FOR OPERATION

*Gangrene* — Gangrene in a pulseless, painful foot is an indication for amputation, unless it is superficial and limited to the tip of a digit and shows evidence of healing without pain at the end of two weeks' hospital treatment consisting of rest in bed (with opiates for the first week if necessary), Buerger exercises and treatment of the local lesion

*Pain Without Actual Gangrene* — The painful, pulseless foot that after two weeks of hospital treatment is unrelieved has insufficient blood supply to be of use, and should be treated by amputation

*Osteomyelitis of a Phalanx* — Osteomyelitis of a phalanx is an indication for operation. Any unhealed ulcer of two weeks' duration overlying or on one side of an interphalangeal joint is regarded as actual or potential osteomyelitis. A positive diagnosis can be made earlier by demonstrating bare bone with a small probe than by the use of x-rays

*Recurring Ulcer* — The patient who has a recurring ulcer in a callus on a toe which, with proper care of the feet, cannot be kept healed is more safely treated by amputation of the toe than by conservative treatment

*Extensive Infection* — Extensive infection is an indication for operation

#### SELECTION OF THE TYPE OF OPERATION

The visualization of the arterial background of the limb is essential to the proper handling of a patient with a circulatory condition. If all peripheral vessels pulsate, this is not difficult. The extent of the local lesion, however, is of little help. There may be complete gangrene of a toe, yet a good result may be obtained by proper local amputation, whereas a toe without gangrene but with a painful ulcer may require an amputation through the thigh for relief. Figure 4 represents (*A* and *B*) legs amputated for gangrene. Figure 4 *A* shows characteristic irregular narrowing of atherosclerotic blood vessels with complete occlusion of all three vessels to the foot. It is therefore obvious that in this type of leg any operative procedure, to be successful, must be done through a point well supplied by the main vessels. Figure 4 *B*, on the other hand, shows no filling of consequence in the main blood vessels, but shows an extraordinary development of collateral vessels. This type of leg, which is warm and of fairly good color, without a definite line of temperature change, offers possibilities of local operative procedures below the level of any main blood vessel. In fact, highly developed circulation of this type is a better background for a Gritti-Stokes amputation than a good popliteal artery with few collaterals.





Fig 4 (case 28863) — *A*, low thigh amputation in a patient, aged 72, for gangrene of the first, second and fourth toes. Injection of the femoral artery with a fine suspension of barium sulphate. Note the irregularity of the lumen of each main vessel, the abrupt ending of the injection at *a*, *b* and *c* due to an occluding thrombus. Note also to what a slight degree the collateral circulation has been developed. (The illustration is from McKittrick and Root, *Diabetic Surgery*, Philadelphia, Lea & Febiger, 1928.)

*B* (case 42419), unsuccessful amputation of the fifth toe for gangrene followed by Gritti-Stokes amputation with a good result in a man, aged 67. Injection of the amputated limb with a fine suspension of barium sulphate showing extensive development of collateral circulation.

## INDICATIONS FOR THE AMPUTATION OF ONE OR MORE TOES

Any local amputation in the absence of pulsation in the dorsalis pedis artery must be undertaken only after careful consideration. The high mortality of patients with reamputations<sup>7</sup> comes from ill advised amputations of toes in feet with insufficient circulation to prevent infection of the blood stream. In general, amputation of one or more toes may be tried for: (1) Gangrene of a toe or portion of a toe, with good pulsation in the dorsalis pedis artery and a warm foot. Occasionally, in the absence of such pulsation, a patient having a toe with a gangrenous tip resulting from trauma will do well after amputation of the toe, if the foot is warm, of good color and with no definite level of temperature change. (2) Osteomyelitis of a phalanx without gangrene. (3) Chronic ulcera-

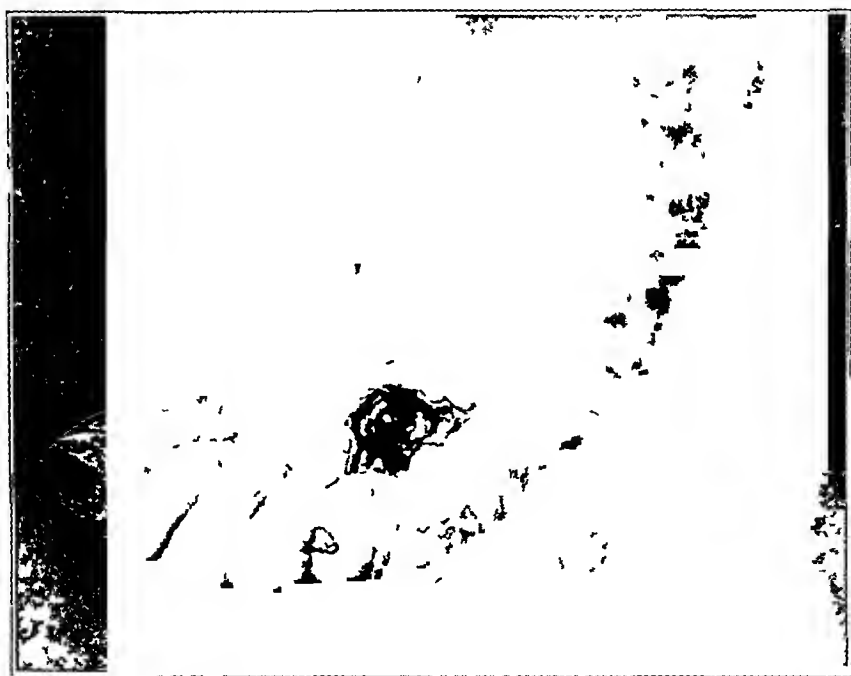


Fig 5 (case 30128) —Gangrenous slough on the dorsum of the foot with extension of the infection between the third and fourth metatarsals in a woman, aged 76. Dorsal incision was used. (McKittrick and Root: *Diabetic Surgery*, Philadelphia, Lea & Febiger, 1928.)

tion in a corn or callus that fails to remain healed under conservative treatment. (4) More complete drainage in cases of infection between toes or involving deeper structures of the foot (figs 5, 6 and 7).

## AMPUTATION THROUGH THE LOWER LEG

The great advantage of an amputation through the lower leg is that gained from preservation of the use of the knee joint. Amputation through the lower leg can be done more frequently than is desirable

<sup>7</sup> Eliason and Wright. *Surg Gynec Obst* 42: 753, 1926.

because of the susceptibility of such a stump to pressure sores. It is a rational surgical procedure if the patient is in good general condition without a rapidly spreading infection and if (1) the skin of the leg is warm and of good color to the level of the ankle, (2) there is good pulsation in the popliteal artery and (3) there is no evidence of lymphangitis or phlebitis above the ankle.

When all of these conditions are fulfilled, it is the operation of choice in (1) a woman under 60 years of age, unless from economic necessity



Fig. 6 (case 30128) —The same foot as that in figure 5, showing operative wound. Removal of third, fourth and fifth toes with portions of the third and fourth metatarsals was necessary for proper drainage. (McKittrick and Root *Diabetic Surgery*, Philadelphia, Lea & Febiger, 1928)

she must be on her feet most of the day, (2) a man under 55 years of age, if operation is done because of a localized infection and not for gangrene and provided he lives relatively near an artificial limb-maker and his occupation does not make it necessary for him to be on his feet for long periods of time (see indications for Gritti-Stokes amputation) and (3) a patient in whom the condition of the other foot is such that

subsequent trouble seems probable. In the latter case, it may be advisable to do an amputation through the lower part of the leg at the first operation for fear that a higher amputation may be needed eventually on the opposite side. Probably the best combination in a double amputation is an amputation through the lower part of the leg on both sides or a Gritti-Stokes amputation on one side and an amputation through the lower part of the leg on the other.

#### GRITTI-STOKES AMPUTATION

From the point of view of service, a Gritti-Stokes amputation gives the most efficient stump above the level of a Symes amputation. The



Fig 7 (case 30128) —The same foot as that in figure 6, showing the end-result eight weeks after operation. Good anatomic and functional result. (McKittrick and Root. *Diabetic Surgery*, Philadelphia, Lea & Febiger, 1928.)

operation is a little more complicated than an amputation through the thigh, the blood supply to the flaps is not so good, and healing is a little more irregular. The surgical requirements for a Gritti-Stokes amputation are (1) good pulsation in the popliteal artery or unusual collateral circulation, evidenced by warm skin and good color to the level of the ankle, (2) absence of lymphangitis, phlebitis or other signs of infection.

to a point at least 3 inches (7.5 cm) below the level of the tibial spine, (3) no clinical or bacteriologic evidence of a general septicemia, and (4) a patient whose general condition suggests the probability of his using some type of artificial limb.

If all of the conditions enumerated are fulfilled, this operation is indicated in (1) a patient who has an amputation done because of deficient circulation, particularly if that patient must earn a living on his feet, (2) a patient who wishes to have a stump free from trouble at the expense of a more normal gait, and (3) an elderly patient who, because of the confidence and the comfort inspired by a long, end-bearing stump, might be able to get around on a peg leg, rather than be confined to a wheel chair.

#### AMPUTATION THROUGH THE THIGH

The indications for an amputation through the thigh are (1) a condition permitting primary suture and requiring the shortest and swiftest operation, (2) conditions that will prevent subsequent use of an artificial limb, such as failing eyesight (not due to cataracts), mental instability, etc., (3) inability to feel any popliteal pulsation, unless the skin is warm and of good color at least to the level of the ankle, (4) failure to palpate the femoral artery in the groin, and (5) extensive infection which makes lower amputation unwise.

#### GUILLOTINE AMPUTATION

By this operation, we mean the classic guillotine procedure. Skin, muscles and bone are all cut in the same plane, the operation being done quickly with minimum manipulation. Dakin's tubes are sutured over the end of the stump, and irrigations are begun at once and continued every two hours. The amputation should be done above the gross infection (not above lymphangitis) through tissue with good circulation, usually through the upper third of the lower leg. In every instance except when amputation is above the knee, a reamputation is done within two or three weeks, if the patient does well. A patient whose response to a guillotine amputation is satisfactory has a sudden and permanent fall in temperature to or slightly above normal (fig. 2). If the response is otherwise, secondary infection is usually present and reamputation should be done only after every possible effort has been made to find a source of infection to explain the failure to obtain the desired response. Compare figures 8 and 2.

The use of the guillotine amputation is restricted to (1) the patient with septicemia, actual or suspected, from a badly infected or gangrenous foot, (2) the very sick patient with extensive sepsis, and (3) the patient who has a gangrenous foot with extensive lymphangitis, in whose case primary suture would be unsafe.

## ANESTHESIA

Spinal anesthesia obtained with procaine hydrochloride<sup>8</sup> has been the anesthesia of choice although that obtained with ethylene and oxygen or with nitrous oxide and oxygen has proved satisfactory for the shorter operations. Ether or chloroform should never be given, and procaine hydrochloride locally only in carefully selected cases in which the local circulation is good and in which injection can be made proximal to any infection that may be present. Our own tendency has been to use more

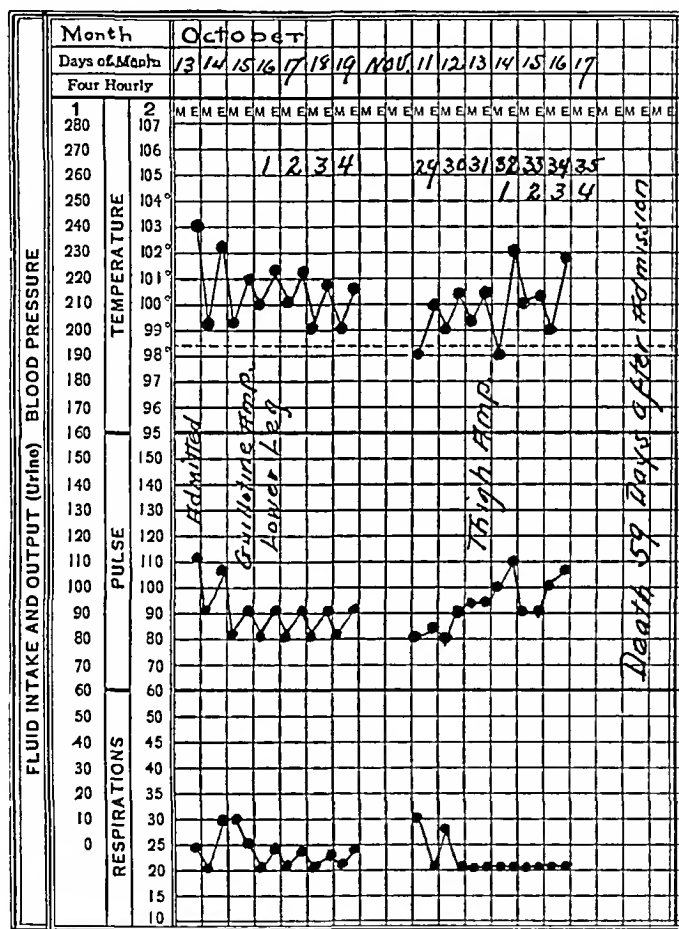


Fig 8 (case 51185) —A chart showing the postoperative course of a man, aged 68, who had gangrene, infection and lymphangitis to the knee on admission to the hospital. Blood cultures disclosed *Streptococcus hemolyticus*. All subsequent blood cultures were negative. The failure of the temperature to become and remain normal after guillotine amputation is suggestive of infection elsewhere than in the stump. The failure to find this resulted in reamputation (through the thigh) thirty-one days later, with breaking down of the stump and death thirty days later. Autopsy showed a left subdiaphragmatic abscess and a small localized empyema on the left.

<sup>8</sup> We still prefer the "C" tablets of procain (Metz), according to the technic previously described (McKittrick, L. S. and Root, H. F. *Diabetic Surgery*, Philadelphia: Lea & Febiger, 1928, p. 86).

rather than less spinal anesthesia even for simple toe amputations. In this series of cases, no patient had a reaction of sufficient severity to warrant any type of stimulation. Except for an occasional case, the level of anesthesia does not go above the crest of the ileum, and for operations in the foot, rarely above the knee. Safety and satisfaction, however, come not so much from the type of solution used as from the experience of the one who gives it. We prefer not to use any preoperative opiate.

#### TECHNICAL POINTS

In diabetic patients, operative procedures, to be successful, must be based on certain fundamental principles. 1. Circulation must be adequate to localize infection and permit repair to take place. 2. Drainage must be dependent and complete. A continuous incision is preferable to counter incisions (fig 9). 3. Incisions must be so placed as to minimize interference with the blood supply and, at the same time, permit extension of the wound should further infection occur.

#### AMPUTATION OF ONE OR MORE TOES WITHOUT DRAINAGE OF THE FOOT

The most common lesion requiring local operation on a foot with good circulation is osteomyelitis of a phalanx involving either a joint or the distal phalanx. A lesion of this type is usually of long standing with an established chronic sinus. The acute exacerbations nearly always quiet down on rest in bed and the application of surgical solution of chlorinated soda (Dakin's solution) locally. There is undoubtedly considerable local immunity, so that the wound, if amputation is done proximal to the lesion and if the sinus is not opened, can usually be sutured loosely with a fine skin suture, healing resulting in from a week to ten days. Experience has shown that it is better not to close the wound if there is no pulsation in the dorsalis pedis artery or if the sinus has been opened.

Any amputation of a toe for gangrene, regardless of the presence of a patent dorsalis pedis artery, is safer if the wound is loosely packed with dry gauze than if it is sutured.

#### AMPUTATION OF ONE OR MORE TOES WITH DRAINAGE OF THE FOOT

Proper drainage of a foot in which infection has extended into the deeper structures represents the most important phase of a surgical procedure on a diabetic patient. This is of particular note because it occurs in a patient with good circulation, otherwise gangrene and possibly septicemia would have developed. It is also of importance because, if it is not properly done, the process is sure to extend, the diabetic situation becomes worse and, finally, either the loss of a limb or death results.

Grodinsky,<sup>9</sup> by painstaking work on fascial spaces of the foot, made a valuable contribution to surgery of the lower extremities. Not having had the benefit of such a definite anatomic study in the past, we are unable to say how closely the spread of infection has followed the lines he described. We are pleased however, to give support to his suggestion that drainage of these deep infections should be done through an incision other than one on the plantar surface of the foot. The latter is

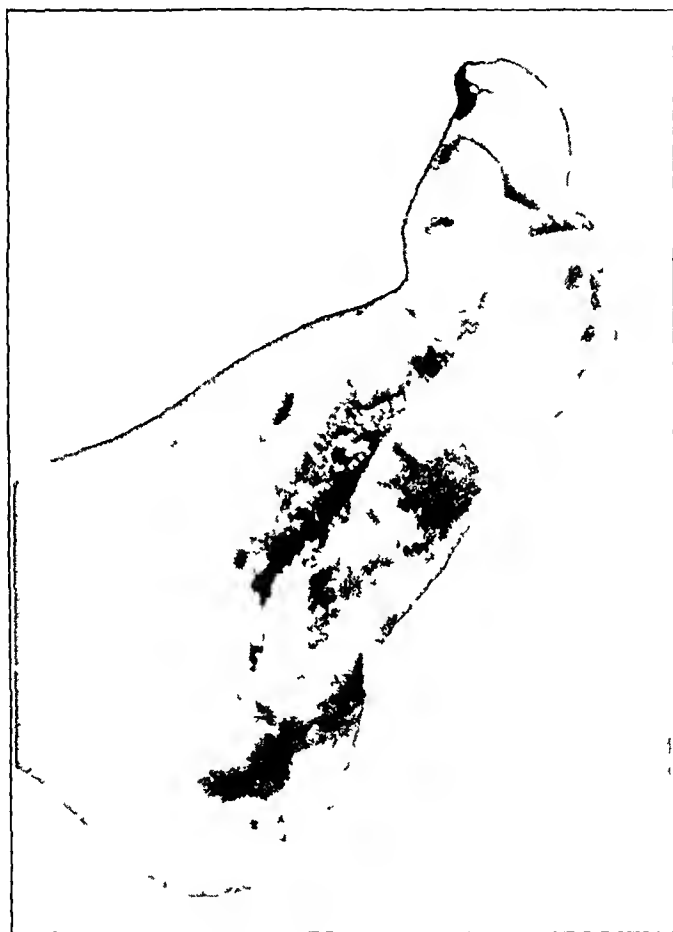


Fig 9 (case 52340) —Extensive infection arising from an ulcer on the lateral aspect of the foot with extension to and destruction of the fifth metatarsophalangeal joint in a man, aged 61. There was also a subcutaneous extension running along under the base of the toes to the medial aspect of the head of the first metatarsal. Note that one continuous incision was used to drain the entire infected area. The fourth toe was not involved, but its removal was necessary in order to insure adequate drainage. There are no counter incisions. A good result was obtained without subsequent operation. See figure 10 A.

all that he said of it unsatisfactory from the point of drainage, bad from the point of scarring and, in addition, conducive to infection of the sub-

<sup>9</sup> Grodinsky, M. Surg Gynec Obst 49 737, 1929



cutaneous tissues of the foot the resistance of which is extremely low. On a sound anatomic basis he recommended the use of a medial incision.

With but few exceptions, we use a racquet type of incision for the amputation of a toe. Ordinarily the aim of the racquet is on the dorsum of the foot. Since October, 1925, we have so placed the incision for amputation of the first toe that whenever there is a possibility that the infection has extended or may extend to the deeper structures of the foot the aim of the racquet is on the medial side of the foot. This part of the incision may then be continued either at the first or at subsequent operations to the inner aspect of the heel, if necessary. Except for the occasional case in which there is unusually good local circulation and in which the infection is still localized within the joint, the head including, if necessary, a portion of the shaft of the metatarsal, is removed. This is beveled in such a way that the base of the wound is smooth with its lowest point nearest the heel. If the infection has extended toward the lateral side of the foot, it is usually advisable to remove the second toe including a portion of its metatarsal in order that the cavity may be sufficiently open to give the complete drainage that is essential. Dakin's tubes are placed at operation, and two-hourly irrigations with surgical solution of chlorinated soda (Dakin's solution) are instituted when the patient reaches the ward. In this way, the submetatarsal area may be satisfactorily drained. In general, the sesamoid bones are removed, always, in case the infection is from a perforating ulcer situated under the head of the first metatarsal.

In cases in which the fifth rather than the first toe is involved, a similar procedure is carried out (figs 9 and 10 *A*). When the incision is along the medial or lateral aspect of the foot it is well to make it more toward the dorsal than toward the plantar surface.

Infection originating from the middle toes is more difficult to drain. In this case we prefer a dorsal incision, removing as many toes as necessary and from the point at which infection is greatest extending the incision as far on the dorsum of the foot as is necessary. Here too free removal of the metatarsals is essential to complete drainage and to make the final wound such that it will drain freely toward its most dependent point (fig 10 *B*).

The drastic removal of bone support in these operations was first undertaken on the basis that a useful though imperfect foot was better than none. Much to our surprise the functional result has been entirely satisfactory, so that we no longer have any hesitancy about removing as much bone as is necessary.

Secondary operations are not infrequent. There may be some extension requiring additional incisions or the removal of more bone. Great care is taken not to break up recently formed adhesions in an effort to hasten separation of sloughing tendons or fascia. Where

clean tendons are cut across, the tendon is left longer than its sheath and a small piece of dry gauze is packed against it in the hope of hastening adhesions to prevent the spread of infection. In all such operative procedures, Dakin's tubes are used, and irrigations every two hours are begun as soon as the patient returns to the ward.

Following operative trauma, there is usually a slight elevation of temperature which should reach normal within a few days and remain so if progress is satisfactory. Any real tenderness in the sole of the foot means extension of infection and will, as a rule, require further operation. Any suggestion of an infection of the blood stream,



Fig 10 A (case 52340) —The same foot as that in figure 9, showing the manner in which the fifth and fourth metatarsals were removed in order to give satisfactory drainage to an infection that had extended from the fifth toe. Note that the fifth metatarsal was made shorter than the fourth and was beveled in order that all parts of the wound should slant to the lowest point.

B (case 36546) —Foot of a patient, aged 51, showing the extent to which the metatarsals were removed in giving drainage to a deep infection from the middle toes. In this case, infection had extended from an infected callus on the ball of the foot through to the dorsum of the foot. The dorsalis pedis was not felt (edema), but circulation was good. A dorsal incision was used. There was involvement of the flexor tendon of the third toe with pus underneath and between the third and fourth metatarsals. Complete healing occurred in two months.

such as chills, lymphangitis and a fever out of proportion to the local sepsis must be met at once with a guillotine amputation through the

upper third of the lower leg. If cases are properly selected, however, and operation carefully done, this complication ought to occur rarely.

### MAJOR AMPUTATIONS

The complete details of major amputations have already been described.<sup>10</sup> A brief résumé of the most important points must therefore suffice at this time.

*Preparation of the Skin*—We are more and more impressed with skin contamination as a cause of postoperative infection of amputation stumps, if *Staphylococcus albus* is to be considered a fair criterion of the source of infection. Preoperative preparation and operative technique are of greatest importance. Whenever possible, the field of operation is prepared by at least one careful scrubbing with tincture of green soap, followed by alcohol and ether and an application of 5 per cent acriflavine in 50 per cent alcohol and acetone.<sup>11</sup> Great care is taken never to scrub or to manipulate the skin more than 2 inches (5 cm.) below the line of incision in the fear, particularly, that such manipulation may stir up an infection in the lymphatics and that gas bacilli may be wiped from the skin in the neighborhood of the gangrenous area into the operative field.

*Tourniquets*—Tourniquets are never used except in guillotine amputations. We fear fresh thrombosis following a trauma sufficient to occlude temporarily the sclerotic blood vessels.

*Flaps*—Equal lateral flaps are used in amputations through the lower part of the leg. A long anterior flap is necessary in a Gritti-Stokes amputation. All amputations through the thigh are done with a circular incision. This minimizes interference with circulation, and the resulting stumps are good. Care is taken to have the fascia come together over the end of the bone snugly, but without undue tension. Hemostasis must be complete but not at the expense of too much manipulation. Precision and a minimum of manipulation are essential. No instrument, sponge or finger allowed to touch the skin inside the wound.

*Nerves*—Absolute alcohol is injected into the nerves as recommended by Lewis and Huber.<sup>12</sup>

*Drainage*—We have followed the teachings of Jones<sup>13</sup> and have closed all of our amputation stumps without drainage, except when a guillotine amputation was done. We believe that this procedure short-

10 McKittrick and Root (footnote 8, p. 168)

11 Tinker, M. B., and Sutton, H. B. Skin Disinfection with Especial Reference to Use of Acriflavine, *J. A. M. A.* 98:1560 (May 14) 1927

12 Huber, G. C., and Lewis, Dean. Amputation Neuromas. Their Development and Prevention, *Arch. Surg.* 1:85 (July) 1920

13 Jones, D. F. Personal communication to the authors

ens convalescence and lessens the possibility of sepsis in the stump and an adherent scar. In each of two series of amputations reported, in which both methods were compared, the results were in favor of stumps not drained.<sup>14</sup>

#### POSTOPERATIVE CARE

It would seem that all possible misfortunes had come to us in the care of this group of patients, infections of the back, varying from small superficial pustules to fatal carbuncles, ordinary sacral pressure sores and, what was probably, the most time-consuming, pressure areas on the remaining heel following amputation requiring weeks of additional hospital care. In an effort to minimize such complications the following routine has been adopted: 1. A balkan frame is attached to each bed as a part of the preparation for amputation. This facilitates movements in bed and lessens the tendency of the patient to push himself up in bed by digging his heel into the mattress. 2. A heavy woolen sock is provided, which affords some protection from pressure, it is removed daily and the foot massaged with hygienic wool fat. 3. A hair pillow, 26 inches by 13 inches by 4 inches, is placed under the leg (or legs) just above the heel to prevent contact between it and the mattress. 4. Ultraviolet rays are applied daily to the back of any patient whose skin shows the slightest evidence of irritation.

In a normal convalescence from an amputation, the dressing of the stump is changed in from six to eight days. Following a Guitti-Stokes amputation, the sutures can usually be removed in ten days. Care must be taken after amputations through the lower part of the leg or the thigh, however, not to remove all the sutures until from ten to fourteen days after operation, and even then it is usually wise to relieve some of the tension by adhesive strips. Continued elevation of temperature to 100.6 F or above, steady pain in the stump, swelling of the limb above the level of amputation or tenderness along the blood vessels are indications for earlier inspection of the dressing. Even then a stump may appear white, soft and dry at the end of three days, whereas in ten days it will be the seat of an extensive infection. If in a patient under suspicion of having septicemia the immediate drop in temperature that occurs after operation is followed by a rise to preoperative level, with but few exceptions the patient either has septicemia or an extensive local infection, probably deep, and all sutures should be removed including those of the fascia unless sufficient sepsis is found in the subcutaneous tissues to explain the temperature and unless removal of skin sutures results in a fall in temperature. Such a wound should be irrigated with Dakin's solution every two hours just as after a guillotine amputation.

14. Ehason and Wright (footnote 7). Kuhns J. and Wilson P. D. Major Amputations. Analysis and Study of End-High Results in 420 Cases. Arch. Surg. 16: 887 (April) 1928.

*Artificial Limbs*—It is our aim to have all patients who have had a Gritti-Stokes amputation and those who have had a routine amputation through the thigh, whom we expect to use artificial legs, walk without direct assistance before leaving the hospital. These patients are measured for temporary peg legs (fig 11). As soon as their stumps and general condition are satisfactory (from ten to twelve days after operation), and they begin to walk with a leg and crutches near the end of the third week. It has been found that if these patients are taught to



Fig 11—Type of peg leg (temporary) used after a Gritti-Stokes amputation or an amputation through the thigh. In the former case, one or more felt pads placed in the bottom of the bucket are used to obtain end-bearing. (This peg leg was made by the Boston Artificial Limb Company.)

walk before going home, they will continue to do so, if not many of the older people content themselves with the wheel chair and crutches. It takes the incentive of going home to stimulate them to a conscientious attempt to learn. Those for whom it seems worth while are fitted with permanent legs when the condition of the stump permits (fig 12). A rule: patients with an amputation are not fitted with temporary legs below the knee until four or five weeks after operation.

## RESULTS OF OPERATIONS

Table 1 represents a summary of operations done by one of us between May, 1923, and Jan 1, 1930. Such a mortality table cannot be interpreted without an understanding of conditions at the time of operation. Suffice it to say that only those patients whose life expectancy seemed to be days rather than weeks were not offered operation (three in the series). All other patients were offered the comfort that amputation of an infected and usually gangrenous leg offered. With but two or

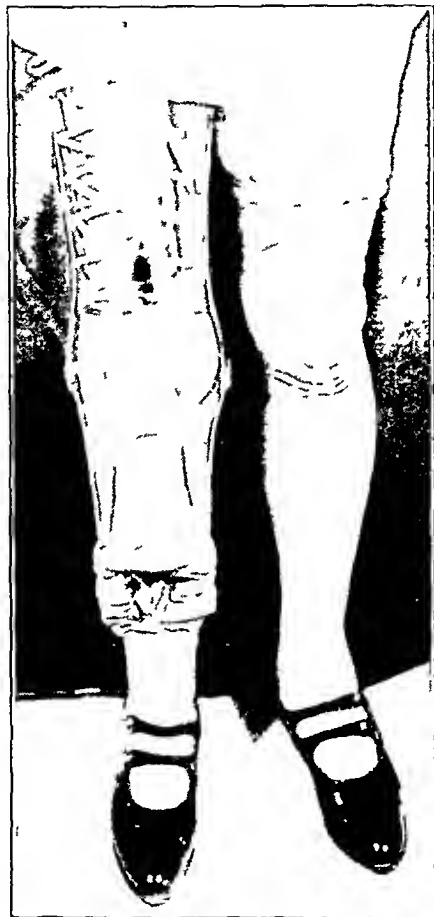


Fig 12—Temporary artificial leg used following an amputation through the upper third of the lower part of the leg. It is modified from the leg described by Wilson (*J Bone & Joint Surg* 4 224, 1922). The bucket is made of leather, and laces in the back in order to take care of shrinkage of the stump. The end is open.

three exceptions, it was accepted. The mortality is high, especially in conditions in which arterial insufficiency is the primary factor. The danger of ill advised delay in this group must be constantly kept in mind in any plan of treatment and every precaution taken to avoid conservative operations in cases in which there is insufficient circulation to warrant it. An effort to save a leg in case 50625 that of a man 72 years of age with a small gangrenous area around the nail cost him sixteen

weeks in the hospital and his life from sepsis. It was realized that he had too little circulation to warrant amputation of the toe, but it was felt that it might be possible for the necrotic tip to separate and heal itself. The distal interphalangeal joint became involved, the removal of the tip of the middle phalanx was followed by extension of infection along the tendon, a Gritti-Stokes amputation, sepsis and death. A Gritti-Stokes operation on this patient when he was first seen would undoubtedly have been successful. This so-called conservative treatment of gangrene has proved unsuccessful in our hands, and we suspect that many patients who do well with this type of treatment would save time with a local amputation properly done. Surely, the patients whom we have seen with actual gangrenous destruction of the tip of a toe that we have not dared to amputate have not responded well to conservative treatment. This

TABLE 1—Operations from 1923 to 1929, Inclusive

Amputation	Number of Cases			Number of Operations	Deaths		
	Gan- grene	Infec- tion	Total		Gan- grene	Infec- tion	Total
One or more toes	14	71	85	90	2 (14.3%)	0	2 (2.3%)
Toe, then major	23	7	30	65	3 (13%)	2 (28.5%)	5 (16.6%)
Through lower leg	10	4	14	15*	0	0	0
Through lower leg, then through thigh	1	0	1	2	0	0	0
Guillotine through lower leg	2	0	2	2	2 (100%)	0	2 (100%)
Guillotine through lower leg, then amputation through thigh	4	0	4	8	2	0	2 (50%)
Guillotine through lower leg, then Gritti Stokes	3	1	4	8	0	0	0
Gritti Stokes	33	2	35	35	5 (15.1%)	0	5 (14.3%)
Gritti Stokes then through thigh	1	0	1	2	1	0	1 (100%)
Through thigh	41	5	46	46	7 (17%)	0	7 (15.2%)
Death under anesthesia, no operation	1	0	1		1	0	1
Total of amputations	133	90	223	273	23 (17.2%)	2 (2.2%)	25 (11.1%)
Incision and drainage	0	8	8	8	0	2 (25%)	2 (25%)
Total of operations	133	98	231	281	23 (17.2%)	4 (4.1%)	27 (11.6%)
Summary of Amputations							
Amputation of one or more toes	14	71	85	90	2 (14.3%)	0	2 (2.3%)
Amputation of one or more toes, including that followed by major operation	37	78	115	155	5 (13.5%)	2 (2.56%)	7 (6.08%)
Major amputation	119	19	138		21 (17.6%)	2 (10.5%)	23 (16.6%)

\* Ligation of popliteal vein preceded amputation

does not include patients who have a small area of superficial gangrenous slough near the tip of a toe, in whom the response to treatment is definite within two weeks.

The relatively few patients who have had an operation on the lower extremity that did not include the removal of one or more toes is noteworthy. This is readily understood when one appreciates the fact that most infections of feet needing operation arise from infection of a toe and that it is only rarely possible to drain adequately a deep infection in a diabetic patient without the additional advantage afforded by the sacrifice of one or more toes.

The patients who have survived a guillotine operation represent lives saved that undoubtedly would have been lost had a primary closure been attempted

From figure 1 it will be seen that more than half (forty-three of eighty-four) of the patients seen during the past year were treated without operation. Almost half of those operated on (seventeen of forty-one) had a successful amputation of one or more toes. Amputation through the lower part of the leg, in 1923 the most frequent operation, has given way to the Gritti-Stokes amputation, not because immediate results are better, but because the resulting stump is more practical. It will also be noted that the increase in number of conservative amputations has been accomplished without increasing the mortality.

TABLE 2—Operations for Bilateral Gangrene from 1923 to 1929, Inclusive

Case	Sex of Patient	Age of Patient		Interval
		At First Operation, Year	At Second Operation, Year	
3210	F	64	65*	1 yr, 3 mo
3745	M	58	63	5 yr
3884	F	70	71	8 mo
3866	M	53	64	11 yr
24133	M	59	60	1 yr
3519	M	63	64	1 yr
3724	F	63	63*	2 mo
5250	M	59	59	3 mo
30875	F	51	51*	3 days
3280	F	64	67	3 yr
4108	M	68	75	7 yr
4721	F	59	60†	1½ yr
4200	F	65	67*	1½ yr
23020	M	70	71	1 yr, 4 mo
42489	F	63	65†	2 yr
43870	M	65	65	3 wk
36970	F	68	70	2 yr
39120	F	59	67†	8 yr
51636	M	68	70†	11 yr
28863	M	72	74*	2 yr
22383	M	68	69*	1 yr
40018	F	69	70*	1 yr

\* Not operated on

† One operation elsewhere

*Reamputations*—There has been an increase in the number of reamputations. Prior to Jan 1, 1927, amputation of one or more toes was followed by a higher operation in six cases, with a mortality of 16.6 per cent. During this period there was no instance of gangrene or infection in the stump from a major amputation requiring reamputation. Between Jan 1, 1927, and Jan 1, 1930, there were twenty-four unsuccessful toe amputations. The mortality has remained the same. This increase in the number of operations without a corresponding increase in the mortality occurred in that group of patients in whom only clinical trial would definitely determine the outcome. Greater experience enlarged the number of patients on whom such a procedure was deemed safe. During this latter period there was one amputation through the upper third of the lower part of the leg following which infection necessitated a guil-



lotine amputation above the knee, and one ill chosen Gritti-Stokes amputation which at the first sign of infection of the stump was followed by a reamputation through the midthigh because of the poor general condition. This stump was solidly healed in twelve days, although the patient finally died of urinary sepsis and renal insufficiency. Eight patients with guillotine amputations survived the initial infection so that reamputation was deemed advisable. Two of these died, one of late metastatic sepsis though his thigh stump was solidly healed, the other, the patient in case 51185, has been mentioned.

TABLE 3—*Causes of Death After Operation for Gangrene or Infection from 1923 to 1929, Inclusive*

Case	Duration of Lesion Before Operation	Amputation	Day of Death		Cause of Death
			Condition	Primary Arterial Insufficiency	
30875	?	Thigh	4		Preoperative streptococcus septicaemia, auricular fibrillation, embolic gangrene in other leg
3798	8 wk	Gritti Stokes	10		Preoperative Streptococcus hemolyticus septicaemia (autopsy)
3036	6 wk	Thigh	4		Preoperative clinical septicaemia, not proved
4820	1 mo	Thigh	53		Stump healed, terminal bronchopneumonia (autopsy)
3971	5 wk	Gritti Stokes	4		Preoperative streptococcus septicaemia
3631	?	Thigh	1		Preoperative streptococcus septicaemia with acute glossitis and pharyngitis (autopsy)
5254	3 wk	Toe	3		Pulmonary embolus (autopsy)
35149	3 mo	Gritti Stokes	7		Infection of stump with gas bacillus (autopsy)
3503	4 wk	Thigh	3		Terminal bronchopneumonia
4326	3 wk	Toe, Gritti Stokes	35		Postoperative streptococcus septicaemia following erysipelas of stump
47311	2 wk	Gritti Stokes	10		Preoperative streptococcus septicaemia
4108	2 mo	(No operation)			Died under ethylene before operation started
6464	3 wk	Guillotine	25		Preoperative general septicaemia
5948	3 wk	Toe, Gritti Stokes	8		Postoperative general septicaemia
45504	?	Thigh	47		Postoperative Staphylococcus aureus septicaemia
45852	?	Gritti Stokes	139		Urinary sepsis plus uremia, stump healed
42589	1 wk	Guillotine	46		Questionable pulmonary embolus (no autopsy)
41994	1 mo	Gritti Stokes	16		Sudden, stump healed
50625	4 wk	Gritti Stokes	44		Postoperative sepsis
51205	2 wk	Thigh	8		Coronary thrombosis, sepsis of stump
51636	6 mo	Thigh	45		Terminal bronchopneumonia
51185	3 wk	Guillotine	57		Preoperative streptococcus septicaemia
Condition Primarily Infection					
4507	?	Toe, thigh	6		Preoperative Staphylococcus aureus septicaemia
3468	16 days	Incision and drainage	9		Postoperative streptococcus septicaemia
43390	5 mo	Toe	15		Coronary thrombosis (autopsy)
45829	?	Guillotine	23		Infection of foot with gas bacillus, plus empyema
31245	?	Toe, Gritti Stokes	64		Sepsis of stump

*Double Amputations*—Amputation of one foot is no contraindication to similar treatment for gangrene of the other. We have numbered among our most grateful patients those who, confined to bed with a painful, foul-smelling gangrene of the remaining foot, have received the comfort offered by amputation. In case 3519, the patient had an amputation through the lower part of the leg performed by Dr D F Jones in September, 1923, after suffering the pain of a gangrenous foot for six weeks. One year later, he returned to the hospital two weeks after a similar accident to his good foot, requesting operation as soon as possible. A Gritti-Stokes amputation was done. The same patient at the age of 69 was able to work in his garden, and in January 1929 he

wrote that he was "feeling better than for years" The number of cases of bilateral gangrene occurring in this series is shown in table 2

Tables 3 and 4 represent the causes of death in these patients It is interesting to note that infection remains the predominating factor, owing either to delay in receiving proper treatment (nine) or to infection following operation (seven) Earlier and better surgical treatment still offers much toward lowering the death rate in these patients

TABLE 4—*Summary of Deaths (Hospital) Following Operations for Gangrene or Infection, from 1923 to 1929, Inclusive*

Cause	Deaths
General septicemia, preoperative	9
General septicemia, postoperative	4
Sepsis, postoperative	3
Infection of stump with gas bacillus	1
Infection of foot with gas bacillus empyema	1
Terminal bronchopneumonia	3
Pulmonary embolus	2*
Coronary thrombosis	2*
Sudden death under anesthesia	1
Cardiorenal disease	1
	<hr/> 27

\* One autopsy

#### SUMMARY

Two hundred eighty-one operations for lesions of the lower extremities in patients with diabetes mellitus form the basis of this report These lesions are classified into (1) those due to arterial insufficiency and (2) those due primarily to infection The importance of such a classification is demonstrated by the results obtained

*Staphylococcus albus* has proved of great importance in operations on diabetic patients It is the organism most frequently found in cases of minor sepsis of the feet and may be the cause of fatal septicemia Gas bacillus infection following amputation for gangrene has been a rare complication in this series Production of gas in wounds infected by staphylococci and streptococci has been frequently seen

The passive exercises of Buerger have proved the most satisfactory method of stimulating circulation

Indications for the various types of operation done are discussed

The 281 operations represent 231 separate conditions with a mortality of 11.6 per cent The mortality in 119 major amputations for conditions primarily due to arterial insufficiency was 17.6 per cent, and in 19 amputations for conditions primarily due to infection was 10.5 per cent, a combined mortality of 16.6 per cent These patients died of the surgical conditions

Spinal anesthesia has been the anesthesia of choice

Early and proper treatment of the surgical lesions will do much to prevent preoperative and postoperative septicemia, the cause of death in 50 per cent of these patients

# SPINAL ANESTHESIA IN THE NEAR EAST\*

P W HARRISON, M D

MUSCAT, ARABIA

Surgical studies and investigations are made more and more in large hospitals where resources are unlimited and assistants numerous. It is evident that there spinal anesthesia has a large place. But much of the world's surgical work is done, and more will be done, far from such centers, as simpler surgical procedures, such as herniotomies and interval appendectomies, are standardized and turned over to the general practitioner.

The surgeon who works with simple equipment and few assistants finds anesthesia his major technical problem. The Mayo Clinic can report the use of general anesthesia in 50,000 cases without a death, but inexperienced anesthetists, at least in the Near East, have a very different record. Moreover, the disadvantages of general anesthesia are not limited to its occasional fatalities. Every surgeon in this part of the world has given artificial respiration dozens of times because his patient had received too much anesthetic, and much more often his aseptic field has been kicked to pieces because the patient had not had enough. Deaths from postoperative hemorrhage are rare, I have not seen one. There has been one death from infection. Most of the unavoidable dangers which still threaten a patient are connected with the anesthesia.

## THE PROBLEMS OF ANESTHESIA

My previous experience with spinal anesthesia was not fortunate. The convenience of the method is obvious, but it was followed some times by very alarming shock and more often by severe headaches, which might last for days, and by paralysis of the bladder requiring long-continued catheterization. Pitkin's articles recalled my attention to this method, and from them as a foundation, I have developed a procedure which seems satisfactory even in this primitive country, so it may be worth reporting. Spinal anesthesia is now used for practically all work below the diaphragm. The subject divided itself into six separate problems.

1 *The Spinal Puncture*—It is not always easy to introduce the needle. Twice I was defeated in spite of all efforts. The interspinous ligament is tough, and it is difficult to keep the needle in the median plane while passing through it. On the basis of an idea that came from

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\* Submitted for publication, March 14, 1930

the Lahey Clinic in Boston, the guide shown in figure 1 was made. After careful anesthetization of the skin and the structures under it, this guide is inserted to a depth of about 3 cm, usually between the fourth and fifth lumbar spines. The needle is then introduced through the guide and pushed forward until it enters the subarachnoid space. This guide has made the spinal puncture a more precise maneuver than before. For the uncooperative patient who bends backward instead of forward, it is very helpful.

It has also made possible the use of needles finer than would be safe otherwise. No effort is made to force a long thin needle through tough structures, and the danger of breakage is less. Most of the work has been done with needles of 0.7 mm caliber. I found 0.5 mm needles

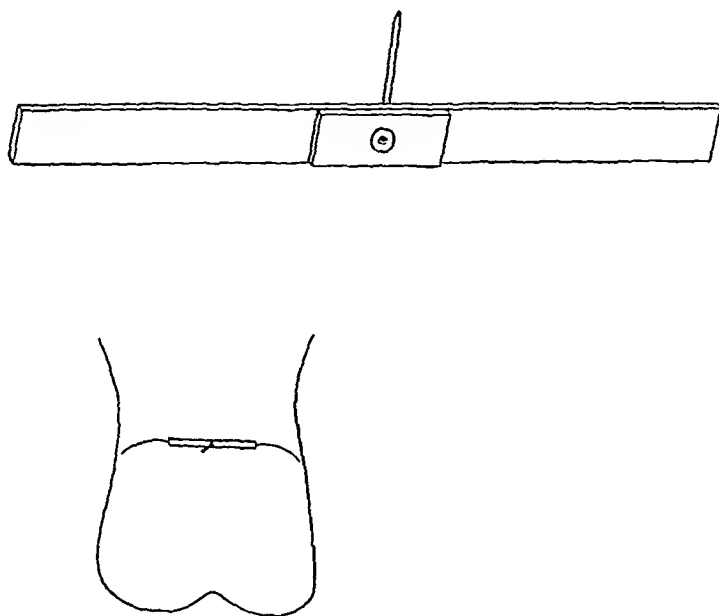


Fig. 1—The upper figure shows the guide for the spinal needle, one-half natural size. The lower figure shows the method of use.

impracticable, because spinal fluid will scarcely flow through so fine a needle, and it was often impossible to tell when the subarachnoid space had been entered. I now use 0.6 mm needles with much satisfaction.<sup>1</sup>

The wound in the dura made by such a needle is trifling. Tested on the cranial dura of a sheep, needles with a long cutting point make a hole which is a simple slit. Needles with a short bevel make a slit that is slightly curved. Holes made with the needles described have to be studied with a magnifying glass. They show the same characteristics as larger ones, but are so tiny that it is impossible to credit them with giving exit to any significant amount of spinal fluid before healing.

<sup>1</sup> All of this instrumentarium can be secured from C. G. Heynemann of Leipzig, Germany.

The only way I could make a trap door opening was by forcing the dull sheath of a trocar through the dura. This leaves a rent, shaped like a half circle, from each end of which extends a short tangent.

2 *The Drug Used*—Benzoyl-dimethyl-aminoethylpropanol hydrochloride (stovaine) has been abandoned as a local anesthetic because of its irritant properties. A 5 per cent solution injected into the skin can cause complete necrosis.<sup>2</sup> However, it has come to be used widely as a spinal anesthetic, and commonly in a 5 per cent solution, which is somewhat diluted of course, in the process of injection. My limited experience with it has not been pleasant. It caused a number of severe paralyzes of the bladder. One of the patients returned home with his control permanently impaired. Procaine hydrochloride and tutocain seem free from such dangers. Tutocain has caused fewer headaches than procaine hydrochloride, but is not entirely reliable. In one of ninety-three cases it failed to produce anesthesia. I regard procaine hydrochloride as the anesthetic of choice.

3 *The Localization of the Anesthesia*—Injected into the subarachnoid space as a simple solution, the anesthetic diffuses somewhat capriciously. Its distribution can be more accurately controlled if it is contained in a heavy viscid medium. The viscosity of such a solution maintains its individuality, and its weight makes possible the shifting of the solution to any desired point in the dural sac by change in the patient's position. I have worked with solutions of dextrose and of cane sugar. Colored with methylene blue (methylthionine chloride, U S P), either solution can be seen to maintain its individuality for hours when placed at the bottom of a glass of water.

The injection of such a solution through a fine needle introduces some complications. The process can be observed in a test tube. With a needle bent at its tip to a right angle, the solution can be injected against the side of the tube. It settles to the bottom of the test tube and is diluted to double its original volume, if the injection has been slow and careful. Injection under high pressure increases the degree of dilution. On coloring the water in the test tube and injecting the anesthetic solution clear, it is found that about a third of the injected solution remains unmixd and of its original strength. This means that when fine needles are used in practical work, about one sixth of the solution in the dural sac is of the original strength, and above this floats a diluted solution the uppermost fraction of which is doubtless very weak.

When injected against the smooth side of a test tube, the resulting dilution is fairly constant. When injected into the spinal canal against

<sup>2</sup> Braun, H. Lokalanesthetics, ed. 3, Leipzig, Johann Ambrosius Bart, 1914, p. 133.

the irregular surface of the cauda equina, the resulting dilution is very inconstant, and efforts to govern the height of the anesthesia by injecting volumes calculated to fill the dural sac to different heights have not been successful. To illustrate, 5 cc of an anesthetic solution was injected between the fourth and fifth lumbar spines in each of three successive patients. The first showed an anesthesia of the anal region, together with a small saddle-shaped area of the adjacent skin. In the second patient, the anesthesia included the lower limbs and the penis. An internal urethrotomy caused no pain. In the third patient, sensation was dulled but not altogether abolished at the middle of the thigh.

This considerable and uncertain dilution of the injected solution is due largely to the fine needle used. With coarse needles and very slow injections, the resulting volume would doubtless be fairly constant, and it might be practicable to govern the extent of the anesthesia by injecting suitable volumes of fluid. I have made no efforts in this direction, because it is easier to locate the solution, and thereby govern the extent of the anesthesia, by adjusting the table on which the patient lies. Barring some exceptional contraindication, the injection is made between the fourth and fifth lumbar spines. The table is tipped up enough to ensure a flow of the solution toward the head, and the patient's head and shoulders are placed on a pillow the height of which governs the point where the solution remains.

From the standpoint of the anesthesia, operations divide themselves into three classes. The first class is made up of those requiring an anesthesia of the perineum and adjacent skin only. Pitkin and his colleagues have used this type of anesthesia successfully in obstetrical cases. I use it for hemorrhoidectomies, excisions of fistulas, etc. Such patients are operated on in perfect comfort, and afterward walk somewhat unsteadily to bed. One cubic centimeter of the solution is allowed to sink to the bottom of the dural sac, and produces the anesthesia. In my experience, 0.5 cc has been insufficient.

The second class of operations is made up of those requiring an anesthesia extending only to the umbilicus. The patients are given a pillow 8 inches (20.32 cm) high, with a slanting support for the back 12 inches (30.48 cm) long. This is usually satisfactory, though some later adjustment is sometimes required.

Most of my operating has been done with this type of anesthesia. It leaves little to be desired for amputations of the lower limbs, hernias, suprapubic operations on the bladder, appendectomies, etc.

The third class of operations consists of those requiring an anesthesia of the upper part of the abdomen. In such cases, the skin must be anesthetized up to the nipple line. Such patients use a lower pillow, 5 or 6 inches (12.7 or 15.24 cm) high, and a slanting support for the back about 8 inches long.

4 *The Duration of the Anesthesia*—One of the greatest defects of spinal anesthesia has been its short and somewhat capricious duration. Previous to this year, I never felt certain of more than half an hour to work in, and on occasion I have had to fall back on general anesthesia within twenty minutes. Surgeons with a better mastery of the method were apparently fairly certain of from fifty minutes to an hour. It would appear from the literature that this is still more or less the situation. If spinal anesthesia is to have any great usefulness, the period must be extended, for the whole current of surgical progress is toward more painstaking and careful, and therefore longer, operations.

To meet the needs of this clinic, three solutions have been developed. First, a solution for operations lasting half an hour or less. In such cases, I use 0.05 Gm. of benzoyl-dimethyl-aminoethylpropanol hydrochloride or tutocain in 1 cc. of a 5 per cent solution of dextrose. This can be depended on for half an hour's anesthesia, it seldom lasts much longer. I use this solution when operating for hemorrhoids, for the excision of anal fistulas, for opening abscesses, etc. The total number of such operations is considerable, and in this limited field such anesthesia is exceedingly satisfactory. Of late I have eliminated benzoyl-dimethyl-aminoethylpropanol hydrochloride in this work.

Theoretically, this duration of half an hour may be due to two factors. It may take thirty minutes to absorb the solution, the anesthesia ceasing when the solution is gone, or conceivably the solution may be absorbed more quickly than this but may leave the drug fixed in the nervous tissues, its effect lasting until it is oxidized or otherwise eliminated. It seemed possible to determine this point. A patient who was anesthetized to the nipple line was put to bed in a semi-sitting position. Within ten minutes the line of anesthesia had descended to the umbilicus. Terminated as is to be described, an anesthesia produced by tutocain may begin to fade in even less time than that. I concluded that the duration of the anesthesia produced by tutocain is only slightly due to fixation of the drug in the tissues, and that practically the anesthesia lasts as long as the nerves involved are bathed in the solution and no longer.

This seemed to simplify the problem of a longer anesthesia. The quantity of the dextrose solution was increased to 5 cc., and in the hope that absorption might be delayed, its concentration was raised to 10 per cent. The dose of tutocain was increased to 0.1 Gm. This solution of 5 cc. of a 10 per cent solution of dextrose, in which is dissolved 0.1 Gm. of tutocain, justified my hopes. The anesthesia resulting from its introduction has never failed to last an hour and a quarter, and usually lasts an hour and a half. I have seen no evidence of meningeal irritation following its use.

Most of the year's operating has been done with this solution and it has given great satisfaction. For hernias, appendectomies, amputa-

tions, work on the bladder, etc., the time afforded is adequate, even though the operator gives the anesthetic solution himself before scrubbing up, and thus the first fifteen minutes of the anesthesia are lost.

This solution is satisfactory for most operations, but not for all. Splenectomies, work on the bile ducts, severe gastric operations, etc. are done infrequently, but double hernias are common, and they require a longer period of anesthesia than this solution affords. In the effort to lengthen the anesthesia further, the use of tutocain was stopped and that of procaine hydrochloride was begun. This drug apparently becomes fixed in the nervous tissues when used as a spinal anesthetic. In such an experiment as that described, after elevation of the head, the anesthetic level does not drop until after about twenty or twenty-five minutes.

Cane sugar was also used in the place of the dextrose, in the hope that its larger molecule might make absorption slower. Procaine hydrochloride is only about half as powerful an anesthetic as tutocain, but it is perhaps three times less toxic. I therefore felt safe in raising the dose to 5 grains (0.324 Gm.). This solution, 5 cc. of a 10 per cent solution of cane sugar in which 5 grains of procaine hydrochloride is dissolved, also proved a success. The anesthesia resulting from its introduction can be depended on for two hours and usually lasts a little longer.

For a prolonged anesthesia of the upper part of the abdomen I do not inject the solution through a 0.6 mm. needle. When such a needle is used, the upper zone of anesthesia may last from only an hour to an hour and a half, while the lower zone persists to the full expected time. The reason for this is undoubtedly the character of the dilution caused by injection through a very fine needle. This has been discussed. I have had no such trouble when using 0.7 or 0.8 mm. needles.

The demands of this clinic are satisfied by these three solutions, and no effort has been made to develop anything further. It is possible that a new local anesthetic recently introduced in Germany may provide anesthetics lasting five and six hours, if its use as a spinal anesthesia proves safe.

During the past year I saw two patients whose anesthesia lasted for hours in a somewhat alarming way. Although they seemed none the worse for the experience, it was disquieting. Much more often I see patients whose condition makes it desirable to terminate the anesthesia as promptly as possible after the operative work has been finished. These, of course, are the patients whose blood pressure has not been stabilized adequately. I have found that a spinal anesthesia can be terminated very simply by injecting 4 ounces (118.4 cc.) of a 5 per cent salt solution intravenously. This idea comes from Dr. Cushing's clinic, where the same thing is done to reduce intracranial pressure. Anesthesia



produced by tutocain begins to fade within five minutes after such an injection, and rapidly disappears. I have had occasion to use this procedure in four such cases, with uniform success. Anesthesias produced by procaine hydrochloride begin to fade after from twenty to twenty-five minutes, and within the following twenty minutes sensation returns over the upper part of the anesthetic area. When 4 ounces of the solution is used, the lower part of the anesthetic area, especially the legs and feet, regain their sensation more slowly. When 8 ounces (236 cc) is injected or the percentage is raised to 10, the effect is more rapid, but in two cases in which this was done the reaction following was severe. I have had occasion to terminate an anesthesia produced by procaine hydrochloride in this way nine times, and have found the procedure valuable.

These results suggested that the injection of 4 ounces of distilled water just before inducing spinal anesthesia might prolong its duration, but in the single case in which the experiment was tried it completely failed to have any such effect.

5 *Stabilizing the Blood Pressure*—Up to this time the effort to stabilize the patient's blood pressure while he is under a spinal anesthetic has been associated with and somewhat handicapped by the effort to prevent respiratory paralysis, which it is assumed will occur if the anesthetic solution reaches and paralyzes the phrenic nerves. It would seem obvious that this might occur. The solutions used paralyze the muscles of the lower limbs and of the abdominal wall. It is true that this motor paralysis is frequently incomplete. Evidently the sensory nerves are more readily affected by the solution than the motor nerves. But the motor roots are involved in all cases. If they were not, the patient could walk back to bed. The danger would seem to be self-evident, and moreover, at the best, the diffusion upward of the anesthetic is under imperfect control. The surgeon lacking all apparatus for maintaining artificial respiration has the feeling that he is walking on the edge of a precipice.

Apparently the self-evident conclusion is wrong. Le Riche and Labat have long since interpreted these cases of "respiratory paralysis" as cerebral anemia due to low blood pressure. Far more convincing is the recent work of Koster and Kasman,<sup>3</sup> who showed that a 2.5 per cent solution of procaine hydrochloride applied to the medulla of a cat has no influence on the respiratory movements. Two and one-half per cent is a strong solution, and if this work is confirmed and it can be determined that the human tissues are no more susceptible than those of the cat, there would seem to be no reason why plastic operations on the nose cannot be done easily and safely under spinal anesthesia. In

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3 Koster H. and Kasman L. P. *Surg Gynec Obst* 49:617 (Dec) 1920

this clinic, work is done with a 6 per cent solution of procaine hydrochloride, and after injection a fraction remains at that strength, while most of it must be above the 2.5 per cent used by these authors. It seemed worth while to ascertain what effect such a solution might have when applied to the medulla.

Two goats weighing 42 and 30 pounds (19.1 and 13.6 Kg), respectively, were each given intraspinally 4 cc of a 10 per cent solution of cane sugar in which was dissolved 4 grains of procaine hydrochloride. They were immediately hung up by the heels, and remained suspended for five minutes, after which time they were laid on the floor. Both of these animals showed complete paralysis of their hind legs, and nearly complete paralysis of their forelegs. Their voices were almost lost so that they could bleat only in a sort of a whisper. The entire body, including the face, was anesthetic, with the exception of the ears, which remained unaffected. Respirations were quiet and with the animal lying motionless on the floor were shallow, but pinching the ear with a hemostat gave rise to active and exaggerated respirations. After about an hour and a half the animals got up and stood on their feet more or less unsteadily, and shortly thereafter the effects of the anesthetic disappeared. A 10 pound (4.5 Kg) gazelle that was given 2 cc of this solution died after a suspension of three minutes. He died in the midst of spasmodic, irregular movements and apparently not from primary respiratory paralysis. It would seem that the danger of respiratory paralysis is not so immediate as was supposed. It will doubtless be possible to work out this point accurately and to eliminate all risk of respiratory paralysis.

The danger of respiratory paralysis may be fictitious, but the danger of falling blood pressure is not. It is this more than anything else that frightened operators away from spinal anesthesia in the past. The present revival of its use is due largely to the introduction of ephedrine, which has gained wide use as a stabilizer of the blood pressure in these cases.

Anesthesias confined to the perineum have no effect on the blood pressure. In thirty-four such operations, I have had no trouble. When the anesthesia reaches to the umbilicus, the patient's blood pressure requires some stabilizing. For these cases, I use from  $\frac{3}{4}$  to 1 grain (0.0486 to 0.065 Gm) of ephedrine, given subcutaneously just before the operation. This answers the purpose very well. Of eighty-three such cases only one required some epinephrine to reinforce the blood pressure during the operation.

Work in the upper part of the abdomen, however, still presents serious problems. To abolish sensation completely the fourth thoracic

segment must be reached, and the skin up to the nipple line will be made insensitive. The whole splanchnic area and everything below it have their vasomotor tone abolished, and it is necessary to supply some adequate external vasoconstrictor stimulus for the whole period during which nervous control is lacking. Up to the present time this has been only imperfectly accomplished. The year's experience included fifty-eight anesthetics reaching to the region of the nipple line. Fifteen of

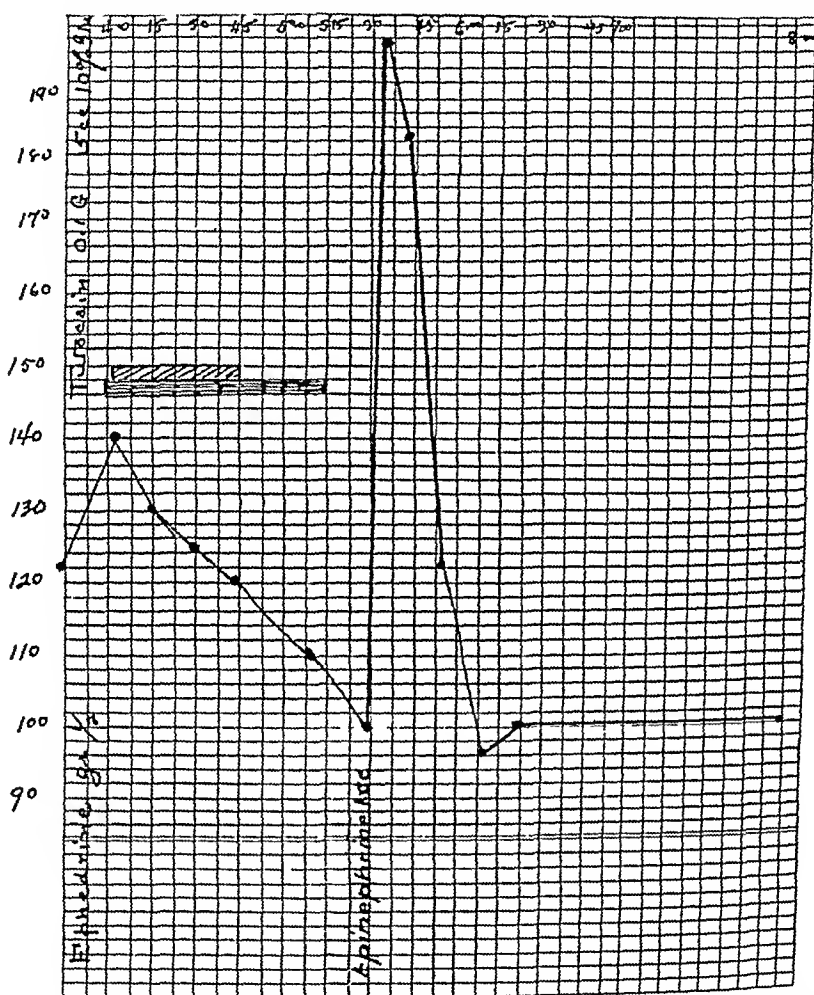


Fig 2—Record of the effect of anesthesia during operation for partial amputation of a foot, Feb 28, 1929. Epinephrine was given to check a threatening drop in the blood pressure. In this and the succeeding figures, the solid shading shows the anesthetic period, the partial shading, the operative period.

these patients vomited during the course of the operation, and four more suffered from nausea. The systolic blood pressure was usually about 60 mm when vomiting occurred. Many of the remainder suffered from a marked drop in the blood pressure. None of these patients died, but it cannot be supposed that such drops in blood pressure are matters of indifference. Adequate means of supporting vascular tone must be developed so that the blood pressure curve will remain normally flat.

I have been unable to discover any method by which ephedrine will accomplish this. Neither massive initial doses nor repeated smaller doses will carry a patient with a high spinal anesthesia through a long operation safely. Epinephrine is a much more powerful drug. I have met no situation in which it was incapable of raising the blood pressure. Figure 2 is an illustration of this capacity. Obviously a drug that can elevate blood pressure in this way is capable of maintaining it, if a

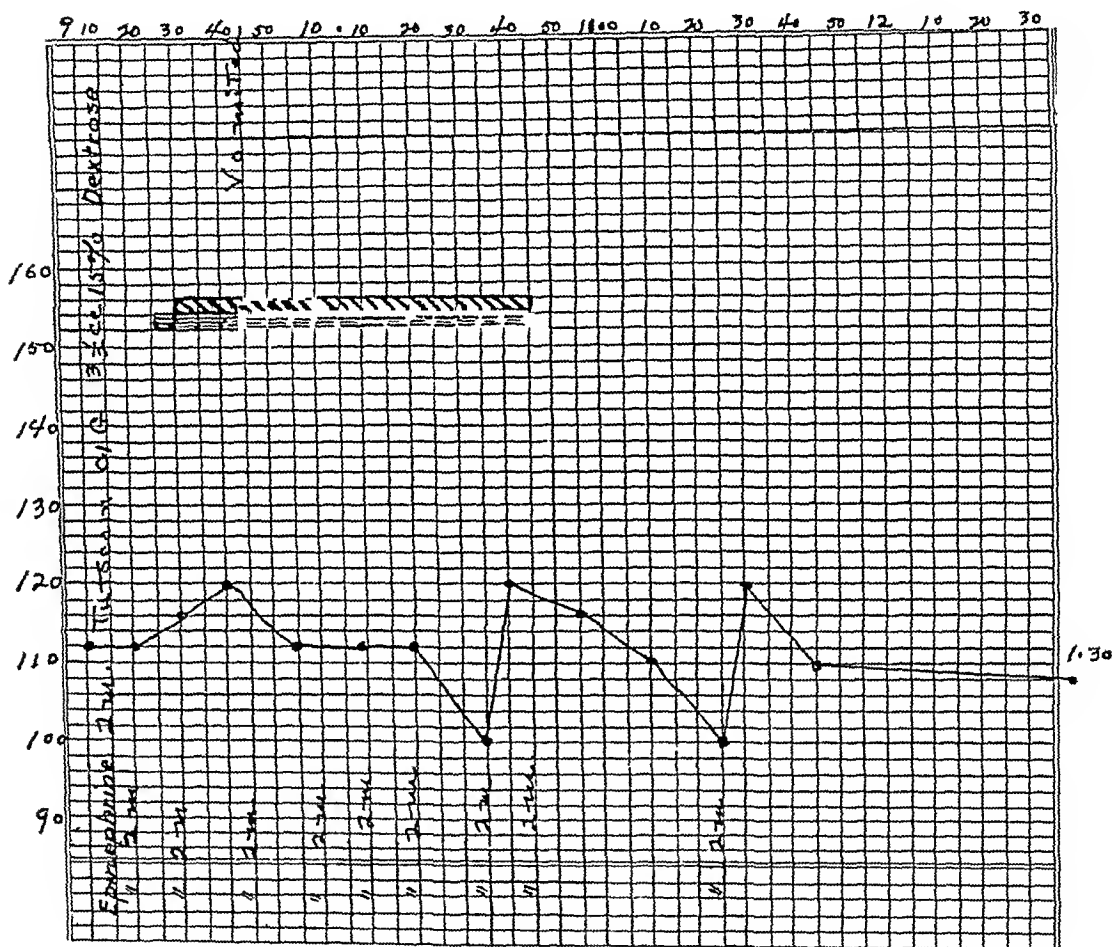


Fig 3—Record of the effect of anesthesia during a difficult operation for hernia, March 27, 1929 Anesthesia extended to the umbilicus The patient was extremely nervous, and fainted during the spinal puncture There was a tendency to a fall in blood pressure, due probably to the extreme mental reaction The situation was controlled fairly well by the administration of epinephrine

suitable method of administration can be devised    Epinephrine seems to be the agent needed

The problem of administration, however, is difficult. Figure 2 illustrates not only the power of this drug, but its exceedingly precipitate and brief action. However, its action seems to last for ten minutes, so that a series of experiments was run in which the blood pressure was

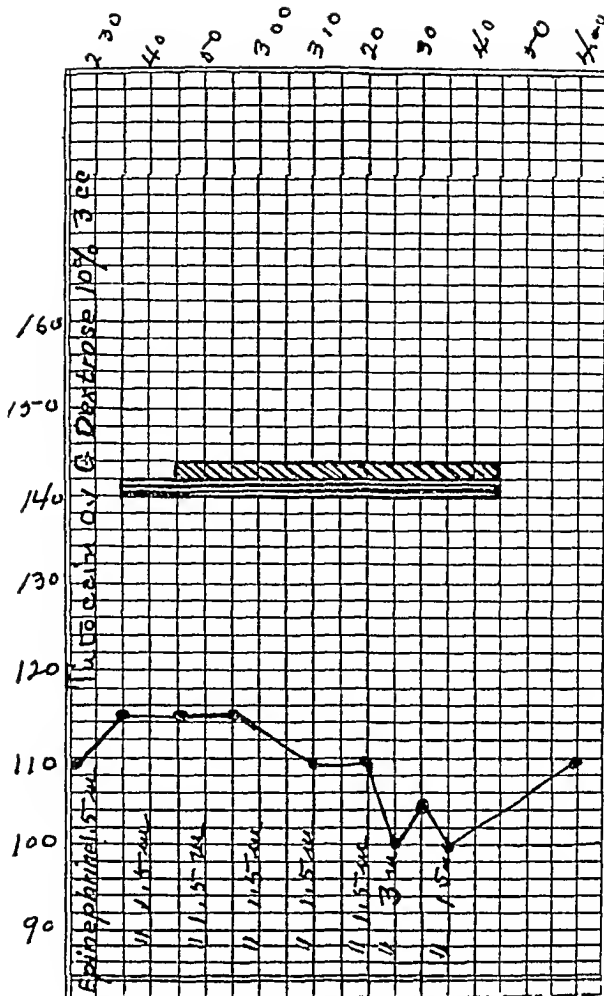


Fig 4—Record of the effect of anesthesia during splenectomy, April 19, 1929. Anesthesia of the diaphragm was not complete. The blood pressure was controlled fairly well by the use of epinephrine.

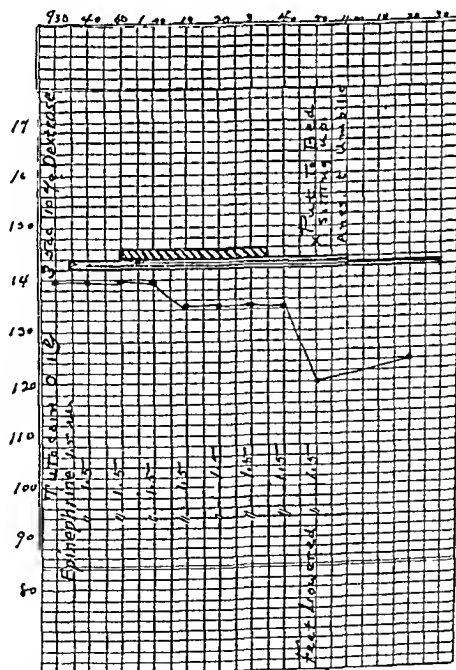


Fig 5—Record of the effect of anesthesia during an operation for hernia, April 25, 1929. Anesthesia extended to the nipple line. The legs were moderately elevated throughout the operation. The drop in blood pressure, which occurred when the legs were lowered, is well shown. On assuming the sitting posture the anesthetic level dropped within ten minutes. The control of blood pressure by epinephrine was fairly effective.

maintained by the injection of 15 minims (0.09 cc) of epinephrine (the commercial 1:1,000 solution) every ten minutes. This was a great improvement, and gave some encouragingly flat blood pressure curves. If the routine dosage proves inadequate, it is a simple matter to increase it. Some irregularities in results apparently were due to capricious absorption from the subcutaneous tissue. I have come to prefer the

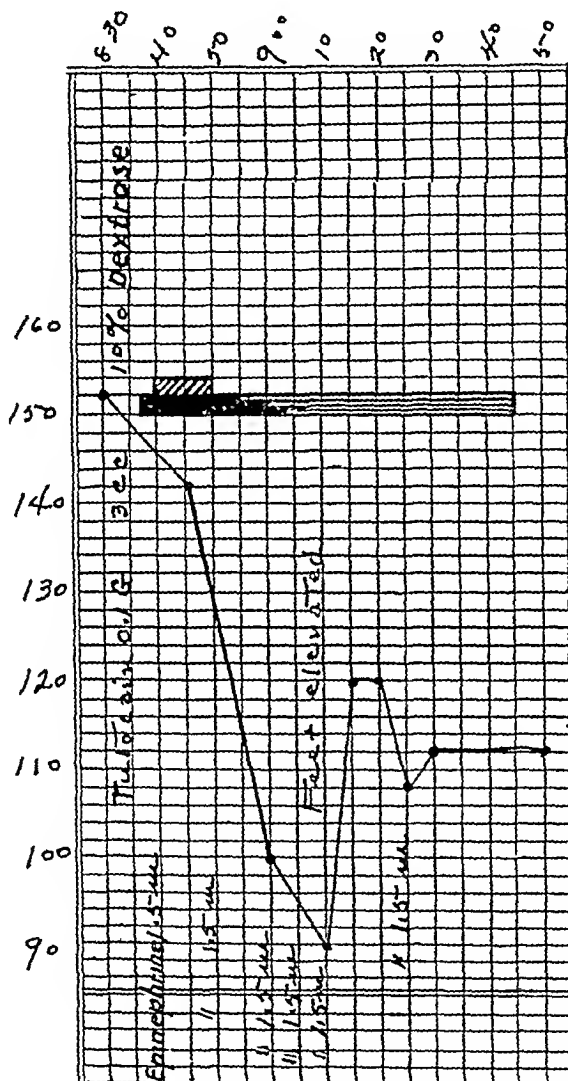


Fig 6—Record of the effect of anesthesia during the clamp and cautery operation for hemorrhoids. The patient was improperly placed. Anesthesia extended to the nipple line. The control of the blood pressure by epinephrine was very poor until the legs were elevated.

intramuscular administration of this drug. Figures 3, 4 and 5 are illustrations of results secured by the administration of epinephrine in this way.

There are some cases in which this method fails to control the blood pressure adequately. In these I have found it of great assistance to

elevate the feet of the patient. The operation is not embarrassed by this procedure. The head and trunk are left undisturbed. Epinephrine plus elevation of the lower limbs has controlled every situation that I have encountered. Figure 6 is the record of such a case.

Profiting by what I have learned of the ability of cane sugar to retard absorption, I ran a small series of experiments in which the blood pressure was maintained by the injection of 1 cc of epinephrine dissolved in 5 cc of a 10 per cent solution of cane sugar. One half of the solution was injected subcutaneously and one-half intramuscularly. This procedure appears to control the blood pressure reliably for one

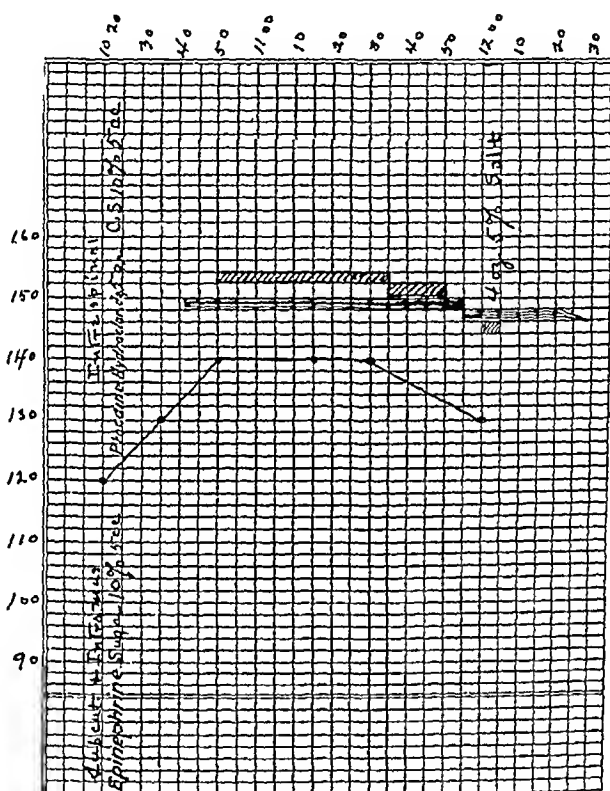


Fig 7—Record of the effect of anesthesia during an operation for hernia in the reclining position, and the clamp and cautery operation for hemorrhoids in the semisitting posture, Jan 8, 1930. There was a descent of the anesthetic level from the umbilicus to the pubic region within twenty minutes after a change in position. The anesthesia was terminated by the intravenous injection of 4 ounces of 5 per cent salt solution. The blood pressure was controlled by 1 cc of epinephrine. Absorption was spread over an hour by means of cane sugar.

hour. At the end of that time, the dose should be repeated. With this method also, there are certain cases that require elevation of the legs. My experience with this method is small as yet, but it seems to promise well. Figures 7 and 8 are charts from such cases.

The repository injections recently reported by Strauch will probably eventually provide just what is needed. By emulsifying epinephrine in

a carefully adjusted medium, he was able to distribute its action over as long a period as was desired. When this method is ready for general use, the problem of stabilizing the blood pressure during spinal anesthesia will probably cause no more trouble.<sup>4</sup>

6 *Postanesthetic Complications*—I have been able to deal fairly well with the situations arising in the course of a spinal anesthesia. Postanesthetic complications have given me more trouble, vomiting is the most frequent. Sometimes it is due to a faulty solution. On a trip

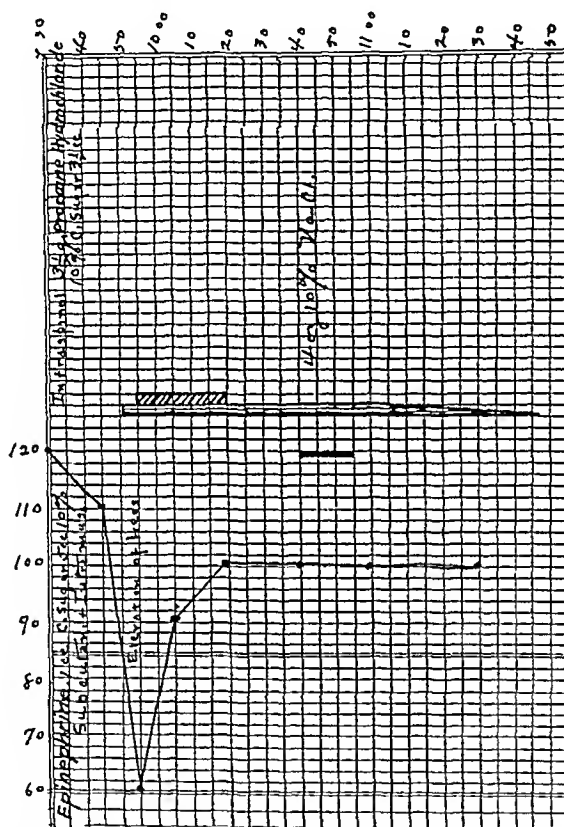


Fig 8—Record of the effect of anesthesia during an internal urethrotomy, Dec 26, 1929. There was an unexpected diffusion upward. Anesthesia extended 3 fingerbreadths above the nipple line. Anesthesia was terminated by an intravenous injection of salt solution. The blood pressure was controlled by 1 cc of epinephrine in 10 per cent solution of cane sugar. The control was very poor until the legs were elevated.

to an outlying district 50 per cent of the patients vomited after the anesthesia. Investigation showed that the distilled water had been run through some old rubber tubing, and the injected solutions were very acid in reaction. A drop of 5 per cent sodium carbonate solution reduced the vomiting to a small fraction of its previous frequency.

4 Stranch, C B. Repository Injections, J A M A 92 1177 (April 6) 1929



Headache is also troublesome, and is usually associated with vomiting. Excluding the period when I was working with solutions that were obviously unsuitable, headaches occurred in about one case in ten. They usually last less than twenty-four hours, and are amenable to acetylsalicylic acid. Severe pains in the limbs occurred in one case.

I find it difficult to believe that these headaches are due to leakage of spinal fluid through a large puncture wound in the dura. I have always used 0.7 mm needles in this work. In the days when I used a simple solution of procaine hydrochloride, headaches were frequent and severe. I use the same needle now and the same drug, but in a heavy solution of cane sugar or dextrose, and with attention to the reaction of the injected solution. Headaches occur now in perhaps 10 per cent of the cases and are of a mild type. The use of 0.5 mm needles did not reduce their frequency.

Two rather distressing fatalities taught me that some impairment of vasomotor tone lasts for a considerable time after the anesthesia has disappeared. Two women with enormous ovarian cysts entered the clinic and were operated on during the same afternoon. One of the cysts weighed 56 pounds (25.4 Kg), the other was estimated at 40 (18.1 Kg). In each case the abdomen was under marked tension. Such cases are fairly common in Arabia. During the past fifteen years the members of this clinic and their immediate neighbors have seen perhaps twenty cases. Barring adhesions, the removal of such a cyst is easy. None of the patients has needed treatment for postoperative shock. These two women were operated on under tutocain anesthesia, 0.1 Gm in 5 cc of 10 per cent dextrose solution. Ephedrine, 1 grain, was given beforehand. Severe shock developed after the operations, in seven hours in one patient and in twenty hours in the other, and they died. Since this experience, I have regarded it as probable that some impairment of vasomotor tone lasts at least through the first twenty-four hours after a spinal anesthesia. I regard as unsuitable for such anesthesia cases in which the operation in itself leaves a damaged vasomotor tone. To add to such damage the further impairment of spinal anesthesia is dangerous.

#### COMMENT

I have come to regard spinal anesthesia as the procedure of choice for surgeons working in the jungle, as well as for those in large centers. There is still, however, a good deal of work to be done in perfecting this method of anesthesia, and the experience of many observers will have to be assembled before all of the questions concerning it are answered.

# THE ETIOLOGY OF NEOPLASMS OF THE BREAST

WITH NOTES ON THEIR RELATION TO OTHER TUMORS OF  
THE REPRODUCTIVE SYSTEM

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NEW YORK

*(Concluded from Page 443)*

## CLINICAL STUDY

The following pages contain a report of the results of a study of 271 women who entered the Memorial Hospital primarily on account of some form of neoplastic disease of the breast. The special object of the analysis of these cases is to afford a rough test of the fitness of the conceptions derived from the preceding theoretical discussion for explaining the origin of a series of typical breast neoplasms. The material used, although relatively small, has been examined with considerable care and it is felt that such an approach by means of a detailed study of a few cases is essential in what must be looked on as a preliminary survey of a rather new field.

The entire group of cases came under my direct observation while the patients were attending one of the outpatient clinics at the Memorial Hospital. The majority were questioned and examined during their first visit to the hospital. When it became evident, however, that this group of patients was yielding a relatively small number of cases in which pathologic specimens were eventually becoming available, about 100 patients were added to the list from the follow-up clinic of the breast department.

## CLASSIFICATION

The general failure of statistical studies to lead to any definite conclusions on the nature of the exciting agent in tumors of the breast may be attributed to the fact that these statistics have invariably been based on a mass of unsorted material. In this paper, therefore, an attempt will be made to classify the cases into groups as morphologically homogeneous as possible and further to subdivide these according to the physiologic condition of the breast under which the tumor appears to have originated.

*Morphologic Classification*—(A) Benign Tumors. One hundred and fifteen benign tumors are included in the study. The examination of the nonmalignant forms is useful, for these forms are at least par-

tially classifiable and the obvious differences in the etiologies of fibro-adenomas and chronic mastitis make apparent the possible differences in origin that may exist in various malignant forms

(1) Fibro-adenomas, characterized by being sharply circumscribed and having histologically a high degree of organization

(2) Painful nodules, the lesion regarded by Moszkowicz as closely related to and possibly the precursor of the fibro-adenoma and shown by Sebening to consist of circumscribed areas of hyperplasia. Cases of this condition are often loosely classified by clinicians as "chronic mastitis," and indeed, in practice, the disease is difficult to delimit from the fibro-adenomas on the one hand and from the diffuse hyperplastic processes on the other

(3) "Chronic mastitis," characterized essentially by a diffuse hyperplasia of the breast epithelium. Under this head have been placed certain cases exhibiting a minor degree of localization of the process as well as the completely generalized lesions

(4) Papillary growths, represented in this study by a few cases of intraductal papilloma and papillary cystadenoma. The number of cases was too small to permit further subdivision

(B) Carcinoma. Criteria are almost entirely lacking for a classification of cases of cancer of the breast from a genetic standpoint. Two theoretical means of genetically subdividing such cases will be considered. In the first place, there is a definite possibility that certain cancers, particularly those in younger women, are derived from or under similar circumstances to the fibro-adenomas, whereas a second group may arise in similar relation to chronic mastitis. The other point of approach is through the study of the different histologic types of cancer of the breast to which special reference is made later

The assignment of a given case to any particular morphologic category has in many instances in the present paper been accomplished on purely clinical grounds since the majority of patients with benign tumors were not considered to require operation and a number of those with malignant growths received only radiation therapy. The latter were advanced or recurrent and there can be little doubt of the diagnosis

It must be noted finally that in the study of tumors one is actually concerned with at least two problems, the origin of neoplasms in general and the reasons for their occurrence in, or evolution through, various stages of cellular undifferentiation. In general, in the following study the divergences from the normal that are common to both benign and malignant tumors are best interpreted as instrumental in the production of neoplasms in general, while differences between statistics on the benign and the malignant series should, theoretically, give a hint to the conditions which produce the variations in cellular differentiation

*Physiologic Classification*—An age classification is nearly essential in the clinical study of tumors for the factor of elapsed time since the period of activity of a hypothetical etiologic agent is most important in evaluating its possible effectiveness in the production of the tumor. Lactation accidents probably have less relation to cancer in women at the age of 70 than at 40 years. Such a classification is of special importance in the breast for in this organ a sharp line is drawn at the menopause marking a complete anatomic and physiologic transformation which is so fundamental that the effects of many previous abnormal stimuli must entirely lose their significance after the change is complete. A history of abnormal menstruation has an entirely different value depending on whether it is found in the present history of a woman developing cancer at 30 or in the past history of a patient with cancer at 60.

The classification adopted which depends on the theoretical state of the ovarian function is as follows:

A<sub>1</sub> Women from puberty to the age of 35 in whom a normal ovarian function should be expected.

A<sub>2</sub> Women from 35 up to 40 years of age, in whom a decline in ovarian activity may be beginning, although evidence of this decline is not to be expected in the normal woman.

B<sub>1</sub> Women over 40 in whom menstrual irregularities have not yet appeared but in whom some physiologic decline in ovarian activity may be assumed.

B<sub>2</sub> Women over 40 who were showing menstrual evidence of approaching menopause at the time of or within a year after the detection of the tumor and those whose final period had occurred less than six months before the detection of the tumor.

B<sub>3</sub> Women over 40 who have ceased to menstruate for from six months to five years, in whom some ovarian activity is probably still present.

C<sub>1</sub> Women from five to ten years past their menopause in whom the effect of the ovary on the breast must at most be a very indirect one.

C<sub>2</sub> Women whose last period lies over ten years behind them in whom ovarian activity has long been apparently extinguished.

In most of the tabulations to be presented, the cases have been recombined into three major physiologic groups, A, B and C, or premenopausal, intramenopausal and postmenopausal, respectively. All cases have, however, been separately charted under the more complicated system, and when differences occurred that are not apparent in the combined totals they will be noted.

In order to make the time relation as accurate as possible, all ages were corrected by subtraction of the known duration from the age given by the patient on admission except in those instances in which a new growth activity had been superimposed on a quiescent tumor of long standing. Yet many growths may have had their microscopic

inception years before the apparent onset. Such a long latent period in the early history of neoplasms is perhaps especially to be considered in the study of old age tumors.

#### AGE INCIDENCE

The pattern of age incidence of any group of tumors has great significance, since the occurrence of a given tumor form in a special age epoch requires the consideration of a possible relationship with the disturbances of function peculiar to that period.

The age table (table 1) gives certain fundamental points.

(A) *Benign Tumors*—Benign tumors are practically limited to the period of ovarian activity. This is a positive observation common to almost all statistics (Primrose, Bunts, Gross), but its immense importance is usually overlooked.

TABLE 1—*Age Incidence*

	Totals	Premenopause		Menopause			Postmenopause	
		Under 35	35-40	10 to Menopause	Menopause	6 Mos.-5 Yrs. After Menopause	5-10 Years Postmenopause	Over 10 Years Postmenopause
Fibro-adenomas	26	18	3	2	1	1	0	1
Painful nodules	22	20	1	0	1	0	0	0
Chronic mastitis	57	22	8	3	17	4	2	1
Papillary growths	11	2	4	0	3	1	1	0
Total benign	116	62	16	5	22	6	3	2
Per cent benign		53.5	13.8	4.3	19.0	5.1	2.6	1.7
Total malignant	155	17	24	18	25	22	24	25
Per cent malignant		11.0	15.5	11.6	16.1	14.2	15.5	16.1

Fibro-adenomas occur characteristically in the very young women (McFarland) and are thus definitely associated with the developmental years of sexual activity. The statistics of Bunts show a second rise in the incidence of fibro-adenomas near the menopause, but this is possibly to be explained as an inclusion in the group of many small, somewhat localized tumors associated with chronic mastitis of the type that Bloodgood designates a nonencapsulated adenoma.

Cases of circumscribed hyperplasia (painful nodules) are found almost exclusively among the young women.

Cases of chronic mastitis are scattered. A large number appear at an early age. This group of patients had many characteristics in common with those suffering from localized painful lumps, and it is possible that a mistake was made in classifying them at all with the chronic mastitis of later years. A second concentration of cases of diffuse "chronic mastitis" occurs in very definite relation to the menopause, the great majority of the patients appearing to be actually in the years of

the "change" Statistics based on cases of chronic mastitis that have come to operation usually emphasize more definitely this high incidence in the years just before the menopause

It is to be noted that it is the tumor with the organic structure resembling in some respects that of the normal breast that occurs in the developmental years, whereas the diffuse hyperplasia is more frequent in the regression period

(B) *Carcinoma*—There is evidence in table 1 also of a relatively high incidence of cancer of the breast in young women as compared with that of many other forms of cancer. A trifle over a fourth (26.5 per cent) of the cases occur before the fortieth year. Two-thirds (68.4 per cent) have occurred before the women have reached a point five years after the menopause and 83.9 per cent have occurred before the menopause has been passed by ten years.

These figures correspond fairly well with the figures that Lane-Clayton listed for America where the age incidence appears to be especially low, while in a collected group of 8,053 cases from many countries, Lane-Clayton's figures show a somewhat higher average age incidence.

The relative frequency of malignancy in young women is a peculiarity which the breast shares with the other organs of the reproductive system, a fact which has been commented on by many writers. Lauterborn, and later Paulsen, using a very large number of statistics, were able to point out that while before the age of 50 cancer affected women far more frequently than men, there was a gradual equalization of the ratio in the sixth decade. This early preponderance in women appeared due to the special quota of cases supplied by the reproductive organs, and as a result Lauterborn concluded that the high early age incidence of cancer in females was due to a disturbance of the internal secretory function of the sex cells. Gade, taking a slightly different point of view, ascribed the frequent development of cancer of the reproductive tract in young women to the earlier senescence of these organs as compared with those of the other body systems. It would be only a minor modification of Lauterborn's theory to suggest that cancer of the breast occurred early because the precancerous lesions from which it is derived develop during the period of ovarian activity and particularly in relation to the menopause.

Cases of carcinoma do occur in considerable number, however, many years after the benign growths have become great rarities. This essential difference in etiology is emphasized by the observation that cancer appearing at the menopause is usually associated with grossly demonstrable chronic mastitis while cancer in an older woman appears usually as an isolated process in a smooth and atrophic breast. From MacCarty's statement that chronic mastitis was present in all of 1,000 cases of can-

cer of the breast, it appears that this benign process never entirely disappears, but the clinical evidence of chronic mastitis in the breasts of older women is nevertheless so slight that the microscopic observations of MacCarty may well represent mere remnants of the hyperplastic tissue formed at or before the menopause

(C) *Sarcoma*—Although cases of sarcoma do not appear in the present study, it is interesting to note that the peak of the sarcoma incidence occurs at a much lower age than does that of carcinoma (GROSS), suggesting the possibility that the former tumors are especially related to the fibro-adenomas, which exhibit an early age incidence and possess often considerable connective tissue activity

#### DEGREE OF BREAST DEVELOPMENT

The various estates relative to marriage and maternity are to be considered in this paper chiefly in the light of their function of producing hypertrophy of the breast, and the history of the course of lactation is to be regarded as indicative of the degree of breast development that has been attained

(A) *Relation of Marriage and Pregnancy to Tumors of the Breast*—The relation of these factors to the tumors of the present group is presented in table 2 A, but since reliable figures on much larger groups of cases exist it is preferable to discuss these

In a total of 14,419 cases of cancer of the breast collected from many different sources, Lane-Clayton found 18.3 per cent single women, as compared with 11 per cent unmarried among 43,022,572 women of over 40 living in the ten countries from which the breast figures were assembled. Hoffman, Simons, Deelman and Crile have each emphasized this relative preference of cancer for the unmarried woman, and Peller attributed to pregnancy a "protective influence" against carcinoma. Lane-Clayton's own study showed the same relative frequency of carcinoma of the breast among single women and pointed furthermore to the fact that among married women the fertility in the cases of cancer was definitely less than that of the noncancerous controls.

The first cited figures, the size of which give them a reliability beyond the hope of any single series, are of tremendous significance. If lactation errors or accidents have anything to do with cancer of the breast, one must wonder why the cases so predisposed have not overbalanced the statistics in favor of the married and fertile women. Cancer of the cervix occurs about fifty times as frequently in married as in single women. Its etiology is strongly influenced by the effects of child-bearing. The supporters of the belief that the inflammations and congestions incidental to childbirth are provocative of cancer of the breast have to explain in the first place the fact that the statistical

TABLE 2—A Breast Development as Result of Marriage and Pregnancy

Percentages Based on Total Women in Classes	Premenopause					Menopause					Postmenopause					Totals				
	Per Cent Lactations Always Normal	Per Cent Lactations Sometimes Normal	Per Cent Lactations Always Subnormal	Per Cent Lactations Never Tried	Per Cent Lactations Always Normal	Per Cent Lactations Sometimes Normal	Per Cent Lactations Always Subnormal	Per Cent Lactations Never Tried	Per Cent of Total With Children	Per Cent Miscarriages Only	Per Cent Married but Sterile	Per Cent, Single	Per Cent of Total With Children	Per Cent Miscarriages Only	Per Cent Married but Sterile	Per Cent, Single	Per Cent of Total With Children	Per Cent Miscarriages Only	Per Cent Married but Sterile	Per Cent, Single
Fibre adenomas	23.8	0	4.8	71.4	50.0	0	0	0	(100.0)	0	0	0	(100.0)	0	0	0	30.8	0	3.8	65.4
Painful nodules	47.7	9.5	9.5	33.3	0	0	0	0	0	0	0	0	(67.0)	0	0	(33.0)	45.7	9.1	13.5	31.7
Chronic mastitis	76.7	3.3	6.7	13.3	79.0	8.7	4.1	0	0	0	0	0	(100.0)	0	0	0	77.1	5.4	7.1	10.7
Papillary growths	66.7	0	16.7	16.7	67.0	(33.0)	0	0	0	0	0	0	(100.0)	0	0	0	70.0	10.0	10.0	10.0
Total benign	53.8	3.9	7.7	34.6	67.7	9.7	9.7	12.9	80.0	0	0	0	71.5	0	0	0	58.7	5.3	7.9	27.5
Total malignant	68.2	0	9.8	22.0	76.6	0	0	12.6	71.5	0	0	0	71.5	0	0	0	72.9	0	11.6	15.5

B Breast Development as Indicated by Functional Capacity in Lactation

Percentages Based on Total Women With Children	Premenopause					Menopause					Postmenopause					Totals				
	Per Cent Lactations Always Normal	Per Cent Lactations Sometimes Normal	Per Cent Lactations Always Subnormal	Per Cent Lactations Never Tried	Per Cent Lactations Always Normal	Per Cent Lactations Sometimes Normal	Per Cent Lactations Always Subnormal	Per Cent Lactations Never Tried	Per Cent Lactations Always Normal	Per Cent Lactations Sometimes Normal	Per Cent Lactations Always Subnormal	Per Cent Lactations Never Tried	Per Cent Lactations Always Normal	Per Cent Lactations Sometimes Normal	Per Cent Lactations Always Subnormal	Per Cent Lactations Never Tried	Per Cent of Total With Children	Per Cent Miscarriages Only	Per Cent Married but Sterile	Per Cent, Single
Fibre-adenomas	20.0	0	60.0	20.0	(50.0)	0	(50.0)	0	(50.0)	0	(100.0)	0	(50.0)	0	(50.0)	0	25.0	12.5	50.0	12.5
Painful nodules	10.0	0	50.0	10.0	50.0	0	0	0	50.0	0	0	0	50.0	0	0	0	40.0	0	50.0	10.0
Chronic mastitis	39.0	31.8	17.4	8.7	50.0	22.2	27.8	0	(50.0)	0	(50.0)	0	(50.0)	0	(50.0)	0	44.2	28.0	23.3	4.7
Papillary growths	25.0	0	75.0	0	(50.0)	0	(50.0)	0	(50.0)	0	(50.0)	0	(50.0)	0	(50.0)	0	29.0	0	71.0	0
Total benign	35.7	19.0	35.7	9.5	50.0	18.2	31.8	0	(25.0)	0	(25.0)	0	(25.0)	0	(25.0)	0	39.4	19.1	35.3	5.9
Total malignant	57.1	17.8	21.4	3.5	48.0	26.0	18.0	8.0	54.3	25.4	20.0	0	54.3	25.4	20.0	0	52.2	21.0	19.4	4.4



relationship here cannot compare with that existing for carcinoma of the cervix, secondly, that there is positively no greater incidence of cancer of the breast in women who have had children and finally that the reverse of what should be expected from a lactation-inflammatory theory is true, namely, that the disease is commoner in single than in married, and in nulliparous than in child-bearing women.

The apparent protective effects of marriage and childbirth may perhaps find their explanations in the following considerations: 1 The women who marry are in general more nearly normal sexually than those who have either no opportunity or no inclination to do so. 2 The physiologic effects of marriage alone and to a greater extent those of pregnancy result in the more complete maturity of the reproductive organs and the elimination of certain minor but perhaps frequent defects of development and function. 3 Sterility in particular is evidence of the existence of abnormalities of the reproductive organs, that may be congenital or acquired, and affect the breast through the ovary.

Examination of table 2 *A* reveals the following points which may be added cautiously to the conclusions drawn from the larger statistics: 1 The fibro-adenomas show a particular tendency to occur among nulliparous women. 2 The so-called "painful nodules" show a somewhat less marked tendency to occur in breasts that have never undergone pregnancy hypertrophy. 3 Cases of chronic mastitis, on the contrary, tend to occur in women who have borne children, a fact corroborative of McFarland's histologic studies on residual lactation acini but contradictory of the reports of certain other writers such as Semb. 4 In the malignant group, the proportion of women who have borne children is at all ages lower than in the chronic mastitis series and higher than in the fibro-adenomas, an observation suggestive of the possibility that cancer may sometimes be related etiologically to the localized and sometimes to the diffuse processes.

As regards both the benign and malignant tumors, relatively many more single women are affected in the early age groups than in the later. This is partly due to the higher percentage of single women at that age in the general population, but it also indicates that in young women, in particular, congenital predispositions may be especially important. For the malignant series it may indicate that in the younger age groups there are more fibro-adenoma derivatives.

(*B*) *Relation of Lactation to Tumors of the Breast*—The importance of the function of lactation in the life history of the breast has made it an obvious field for study and many authors (Leaf, Adair, Lane-Claypon) have found an apparent relation between certain abnormalities of nursing and the development of cancer. Lane-Claypon's survey of the literature on the subject led her to no conclusions, but in her own

studies the cancer group contained a higher percentage of women who had not nursed their children (and also, paradoxically, more who had nursed their children over excessively long periods) than did her control group. She stated that the nonlactation "seems" chiefly due to disinclination on the part of the mother.

(1) *Nursing Failures* In regard to the actual incidence of nursing failures among the women in this series, the following points stand out from a study of tables 2 *B* and 3. 1 If one considers the incidence of lactation failures in reference to all the children borne by the patients with tumor (table 3), it appears that 91.4 per cent of the children of women with benign and 91.7 per cent of the children of women with malignant tumors were nursed for at least a short period and that 69.3 and 77.4 per cent of the respective groups were nursed for at least six months. As a rough control for these percentages may be mentioned the report of Mitchell who found that of 3,000 normal mothers bringing their babies to the Children's Hospital in Philadelphia, 80 per cent had nursed their children for some time and 40 per cent had nursed over six months. It appears, therefore, that the nursing record in these cases of tumor has been excellent. 2 The children of the patients with cancer had been more often successfully nursed than those of any of the patients with benign tumor, but in particular more often than those of patients with fibro-adenoma and "painful nodules." 3 There was scarcely any difference in the incidence of nursing failures in the young as compared with the older cases of cancer.

(2) *Causes of Nursing Failure* According to the special theory of tumor genesis which one has in mind, one may evaluate the history of breast behavior during lactation in terms of congestion and stasis or of development and functional capacity. On account of this divergence in point of view, it is of great importance to note that in the present group of women, by far the commonest cause of failure to nurse normally for at least six months was insufficient milk supply, i. e., inherent physiologic deficiency (table 3). Next to this reason in order of frequency come infantile causes, including stillbirths, then maternal illness, including new pregnancy. Weaning on account of local breast trouble, usually abscess, accounts for a few cases, while the number of children deliberately not nursed, when the physiology of the breast and the health of mother and child permitted it, is almost negligible. About 2 per cent of all children of all groups were thus deliberately refused the breast by the mother.

3 *Nursing Capacity* Since it is clear that at least among the women now under consideration refusal to nurse played essentially no part and a physiologic deficiency was the chief cause of failure to nurse properly, it is necessary to consider in special detail the factor of underdevelopment as manifested by hypogalactia. An idea of the normal incidence

TABLE 3—Causes and Types of Lactation Deficiencies

	Premenopause										Menopause										Age 40 to 5 Years after Cessation									
	No Lactation					Lactation Under 6 Mos					No Lactation					Lactation under 6 Mos					No Lactation					Lactation under 6 Mos				
	Per Cent Normally Nursed	Lack of Milk	Infant Death or Disease	Maternal Illness	Breast Disease	Economic or Dis-inclination	Failure in Supply	Infant Death or Disease	Maternal Illness	Breast Disease	Economic or Dis-inclination	Per Cent Normally Nursed	Lack of Milk	Infant Death or Disease	Maternal Illness	Breast Disease	Economic or Dis-inclination	Failure in Supply	Infant Death or Disease	Maternal Illness	Breast Disease	Economic or Dis-inclination	Per Cent Normally Nursed	Total Children	Complement Feedings	Infant Death or Disease	Maternal Illness	Breast Disease	Economic or Dis-inclination	Complement Feeding Cases
Fibro-adenomas	9	11	0	1	0	0	6	0	0	0	0	50	0	0	0	0	0	0	0	0	0	0	0	4	1	0	0	0	0	0
Painful nodules	13	54	1	1	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chronic mastitis	51	55	1	2	4	0	5	2	3	1	1	75	0	1	0	0	0	6	1	1	0	0	0	60	4	0	0	0	0	5
Papillary growth	8	25	0	0	0	0	1	0	0	0	0	6	0	1	0	0	0	1	0	0	0	0	0	6	5	0	0	0	0	5
Benign	81	47	2	4	4	0	16	2	3	1	1	73	0	2	0	0	0	9	1	0	0	0	0	70	10	0	0	0	0	5
Malignant	66	65	3	0	2	1	13	0	0	0	0	74	1	6	0	0	1	8	2	1	1	1	146	4	4	2	1	1	1	4
Total																														
Postmenopause																														
Over 5 Years Since Cessation																														
Fibro-adenomas	7	86	0	0	0	0	0	0	1	0	0	45	0	1	0	0	0	8	0	1	0	0	0	20	0	0	0	0	0	1
Painful nodules	0											13	1	1	0	0	0	4	0	0	0	0	0	13	0	0	0	0	0	0
Chronic mastitis	4	75	1	0	0	0	0	0	0	0	0	66	2	3	4	0	0	11	3	4	1	2	0	115	0	0	0	0	0	0
Papillary growths	1	0	0	0	1	0	0	0	0	0	0	40	0	1	1	0	0	2	0	0	0	0	0	15	0	0	0	0	0	9
Benign	12	75	1	0	1	0	0	0	1	0	0	60	3	6	5	0	0	25	3	5	1	2	0	163	0	0	0	0	0	5
Malignant	137	72	4	2	2	0	12	1	2	1	1	72	11	9	4	3	3	33	3	6	2	6	1	349	11	3	3	2	6	19

Summary

Per cent of deliveries not followed by any nursing period benign 8.6 malignant 8.3

Per cent of deliveries followed by a nursing period of at least six months benign 69.3 malignant 77.4

Per cent of deliveries followed by subnormal nursing function exclusive of cases merely requiring complementary feeding Primary hypogalactia benign 1.8 malignant 1.1 Secondary hypogalactia benign 1.8

of this condition is given by Lande's figures which showed that of 807 women, 4.5 per cent were unable to nurse at all (primary hypogalactia) and 11 per cent failed within three months. Other writers give somewhat higher figures (Coerper and Werner, Kahn, Winternitz).

A consideration of the incidence of hypogalactia among these women with tumors of the breast shows the following:

1. The total incidence of hypogalactia did not differ greatly from the apparent normal incidence, for the figures for the tumor series were as follows: Primary hypogalactia, benign, 1.8 per cent, malignant, 3.1 per cent, secondary hypogalactia, benign, 15.3 per cent, malignant, 9.4 per cent.
2. There is no reason to believe from the history of their function that the breasts of patients with cancer were inferior developmentally to the benign group, for (a) in table 2 B it is clear that the percentage of women with carcinoma of the breast who, when they made the attempt, were always able to nurse their children is considerably higher than for any of the benign groups, although (b) if one omits the women in whom a full lactation was accomplished at least once, then the number of women in whom complete breast maturity was possible (or in whom on at least one occasion satisfactory drainage was established) is almost exactly the same for all carcinomas and for the cases of chronic cystic mastitis.
3. The cases of fibro-adenoma and "painful nodule" however, give evidence of a probably inherent factor of subnormality by the consistent failure of the breasts of these women to give a proper supply.

*Summary on Lactation*—There is no clinical evidence that the refusal of the mother to nurse has any relation to development of tumors of the breast. There is a little evidence to point toward the belief that women who have a physiologic incapacity to nurse may be particularly predisposed to the development of fibro-adenomas and certain forms of hyperplasia.

#### PREVIOUS BREAST DISEASE

(A) *Engorgement in the Puerperium*—Statistics on this subject are perhaps of little value for moderate engorgement of the breast is a practically normal incident at the onset and termination of lactation, and it is also not clear whether its occurrence in a severe form is to be regarded as significant as a sign of special breast constitution or important as evidence that the breast has been subjected to a period of non-infectious inflammation.

The figures as obtained in this study appear in table 4. There is no apparent difference in the frequency of this condition in the benign and malignant conditions, but in each the history of engorgement is more common in the young women with tumors than among the older.

(B) *Mastitis Puerperialis*—The figures in table 4 show an apparent incidence of mastitis (suppurative and nonsuppurative) of 7.9 per cent.

of all the lactations of the benign group of cases and 71 per cent of the malignant. There is thus apparently no reason to believe that inflammation has anything to do with malignancy as opposed to tumors in general.

As compared with the apparent normal incidence of mastitis, these figures are definitely high. Weber cited the statistics from various modern clinics as varying from 0.64 to 1.93 per cent, although it must be noted that such figures refer as a rule only to the incidence of mastitis while the patient was in the hospital. Older writers, however, such as von Winckel, in 1878, gave 5.9 per cent and Kohler, in 1882, cited 13 per cent. It is probable that the sanitary conditions under which the women of this report bore their children more nearly approximate those on which the older figures are based.

In passing, it is interesting to note that in spite of the general fall in the apparent incidence of puerperal mastitis since von Winckel's day and the improved hygiene of the lactating breast in civilized countries, there has been no evident corresponding fall in the frequency of mammary cancer.

A division of the types of mastitis in the history adds a little more hope of accuracy.

(1) *Nonsuppurative Mastitis*. The apparent occurrence of this disease almost exclusively in the breast affected by the later developing tumor (table 4) is in agreement with the results of Lane-Clayton's studies and gives perhaps some special significance to this feature of the histories. Yet certain reservations must be made. 1. The determination from the history of what should be listed as nonsuppurative mastitis and what engorgement is nearly impossible. It is therefore small wonder that the estimates on the occurrence of mastitis in the history of breast cases have varied from 5.3 to 89 per cent (Lane-Clayton). 2. The localization by the patient of the side in which the mastitis occurred is extremely susceptible to suggestive influences. 3. The fact that nonsuppurative mastitis was a trifle more frequent in the benign than in the malignant series alone detracts from the weight of the evidence, if there be any, that it is in any way related to cancer apart from tumors in general.

(2) *Suppurative Mastitis*. In abscess of the breast one has a definitely determinable subject for historical study since all patients remember an incision. The incidence of abscess of the breast in the history of the women in this study (2.4 per cent of the lactations of the benign series and 3.4 per cent of the malignant series) is apparently somewhat higher than the averages reported by most modern hospitals (Baer and Reis), but as has been noted such reports deal only with women under the most careful supervision and include only the abscesses

TABLE 4—Lactation Accidents

Lactation Per Cent Based on Total Women Mastitis and Abscesses Per Cent Based on Total Births	Premenopause						Menopause						Postmenopause						Total																
	Engorgement			Mastitis			Abscess			Births			Engorgement			Mastitis			Abscess			Births			Engorgement			Mastitis			Abscess				
	No	%		No	%		No	%		No	%		No	%		No	%		No	%		No	%		No	%		No	%						
Fibro adenomas	5	9	3	60	1	11	0	0	0	2	4	1	50	1	25	0	0	0	0	1	7	0	0	0	0	0	0	8	20	1	50	2	10	0	0
Painful nodules	10	13	1	10	1	77	0	0	0	0	0	0	0	0	0	0	0	0	0	10	13	4	40	1	8	0	0	10	13	4	40	1	8	0	0
Chronic mastitis	23	51	11	18	1	80	1	20	18	60	8	41	0	0	3	50	2	4	1	50	0	0	0	0	0	0	43	115	20	46	1	35	1	35	
Papillary tumors	1	8	1	100	2	25	0	0	2	6	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	7	15	4	57	2	13	0	0	
Total benign	42	81	22	52	8	100	1	12	22	70	9	41	1	11	3	43	4	12	1	25	0	0	0	0	0	0	68	163	32	47	9	55	4	24	
Malignant	28	66	13	46	2	30	5	75	50	146	17	31	5	31	3	20	35	137	13	37	6	44	4	30	43	38	113	349	43	38	13	37	12	31	

Summary on breast affected—Mastitis benign, tumor side 8, bilateral, 1, normal, 1 0, malignant, tumor side, 10, bilateral 0, normal, 3  
 Abscess Benign, tumor side 3, bilateral, 0, normal, 1, malignant, tumor side, 7, bilateral, 1 normal 1

of the early puerperium It appears then that the incidence of abscess of the breast among cases of tumor was slightly if at all above that of the general frequency This result agrees with Lane-Claypon's conclusions on her larger series

It should be noted furthermore that of the seven patients with cancer who had a history of abscess in the same breast, three showed the scar in a different quadrant from that of the tumor, two showed no scar and in a sixth a small lump from which the cancer was said to have arisen had preceded the abscess by many years

(C) *Abscess Unrelated to Pregnancy* (table 5) —Six patients, three with benign and three with malignant growths, gave histories of an abscess of the breast when not pregnant This is a very high incidence

TABLE 5 —*Previous Nonpuerperal Breast Disease* \*

	Premenopause		Menopause		Postmenopause		Total	
	Abscess	Previous Tumor	Abscess	Previous Tumor	Abscess	Previous Tumor	Abscess	Previous Tumor
Fibro-adenoma	0	3	0	0	0	1	0	4
Painful nodule	0	1	0	0	0	0	0	1
Chronic mastitis	3	1	0	3	0	2	3	6
Papillary growths	0	0	0	0	0	1	0	1
Benign	3	5	0	3	0	4	3	12
Malignant	1	2	2	2	0	4	3	8

\* Of six nonpuerperal abscesses, four were on normal side, one on tumor side and one undetermined

Previous tumors includes those removed and also certain long existent quiescent lumps out of which a malignant growth appears to have originated

It is not clear whether these abscesses should be regarded as significant from their possible character as inflammations, perhaps tuberculous, or as infected cystic tumors The majority were in the breast unaffected by the later tumors

(D) *Previous Tumors of the Breast* (table 5) —The history of the existence of other tumors prior to the one for which the patient entered the hospital adds considerable to the complexities of localizing the time at which one should seek for the etiologic factor In table 5 are given the combined figures of the patients from whom a tumor of the breast had been previously removed and those in whom the present malignant growth appeared to have originated from a long existent benign one Table 7 shows that many of these growths had been present for a long time

It is noteworthy that the highest frequency of a history of such previous tumors was in the old age group, an observation which to a small degree supports the suggestion that the old age tumors are malignant transformations of benign abnormal tissue the etiologic basis of which lies back during the period of ovarian activity





(E) *Previous Breast Trauma* (table 6) —The possibility that trauma may be capable of initiating abnormal epithelial proliferation in the breast is testified to by certain histologic studies such as those of Bartlett who has reported seven cases of unilateral hypertrophy of the breast before puberty and one in a man over 70, all following an injury. That these breasts, though unilaterally developed, were themselves more or less symmetrically formed makes it appear probable that the trauma was only one of the causes of the growth.

Lane-Clayton's review points out that a history of breast trauma has been found in cases of cancer in from 26 to 44.6 per cent, depending on the observer, and it is quite likely that in any series a persistent questioner could run the figure to nearly 100 per cent. Lane-Clayton's

TABLE 7—*Elapsed Time Since Occurrence of Trauma and Appearance of Previous Tumor*

	Benign											Malignant										
	Time Unknown	Less Than 1 Mo	1 Mo -6 Mos	7 Mos -12 Mos	1 Yr -2 Yrs	3 Yrs -5 Yrs	6-10 Years	11-20 Years	21-30 Years	Over 30 Yrs	Totals	Time Unknown	Less Than 1 Mo	1 Mo -6 Mos	7 Mos -12 Mos	1 Yr -2 Yrs	3 Yrs -5 Yrs	6-10 Years	11-20 Years	21-30 Years	Over 30 Yrs	Totals
Definite trauma	0	2	2	0	1	0	1	1	0	0	7	0	2	1	4	4	1	2	1	0	1	16
Vague trauma	2	3	2	5	3	2	0	1	0	0	19	2	4	4	1	2	5	0	0	0	0	24
Chronic trauma	1	0	0	0	0	0	0	1	0	0	2	10	0	0	0	0	0	0	0	0	0	10
Previous tumors	0	0	0	0	1	1	2	4	1	3	12	0	0	0	0	0	2	3	0	0	2	8

very careful study of this question in which the cases were separated into those with and those without actual bruising of the skin appeared to indicate rather definitely that traumatism played a part in the production of cancer.

The distribution of a history of trauma among the different tumor groups of the present series is presented in table 6. The equal incidence of trauma in cases of carcinoma, fibro-adenoma and "painful nodule," as compared with the much lower incidence in the cases of diffuse chronic mastitis, implies that the presence of a lump may well have the suggestive effect attributed to it, for few authors would ascribe much importance to trauma as a factor in the production of fibro-adenomas. The age distribution of the frequency of trauma shows a strange drop in the group of women who developed cancer near the menopause. The factor of chronic trauma appears chiefly in the oldest group, possibly because women of this age and generation are wearing corsets, but perhaps because in the older women an extrinsic factor is required to start growth.

In general, it must be said, as Dietrich and Frangenheim have pointed out, that if trauma is a factor it is surprising that cancer of the breast is not much more common among the industrial and peasant working classes and much less common among the well to do

#### ABNORMALITIES OF OVARIAN FUNCTION

The possibilities for the studies of an organ's function afforded in the ovary by the phenomenon of menstruation are in a sense unique, for the effect of what may often be minor variations in organic structure, appear at once in the form of definite variations in the interval duration and amount of menstrual flow. Such symptoms are readily translatable into quantitative data by the patient herself and since the constant repetition of the menstrual phenomenon has given her training on the subject and because the necessities of hygiene force the occurrence of changes in type on her consciousness, the testimony of the patient on this subject gives information more accurate than most data similarly obtained.

The majority of the few writers who have sought for it have failed to find a clinical ground for believing that abnormalities of menstruation are in any way connected with cancer of the breast. Simons, although he reported several cases of atypical menses in younger women with carcinoma of the breast, comes to no conclusions in regard to the etiologic relation of menstruation to cancer. Lane-Claypon also reported almost completely negative results, although she stated as her opinion that there may none the less be some relation between menstruation and tumor growth in the breast.

In the present study, the ovarian activity will be analyzed from several angles, based on the following suppositions: 1 The original or characteristic type of menstruation which the patient experienced in her early years of maturity is an index of her normal ovarian constitution. 2 The "present type," namely, that which the patient is experiencing at the time of the tumor's onset is the product of the original constitution and the modifying influences of acquired pelvic disease and the degenerative changes of age. It is in general the more significant of the two since it is under its regime that the tumor has theoretically taken origin. 3 Changes in the type of menstruation indicate a change in the effect of the ovarian secretion on the endometrium and hence probably also on the breast. 4 The character of certain other processes such as puberty and the menopause as well as the symptoms of premenstrual pain and dysmenorrhea give varying indications of the constitution and condition of the reproductive system.

(A) *Puberty, The Onset of Menstruation*—Abnormalities of puberty, particularly that of late onset have been shown to be fre-

quently indicative of genital underdevelopment (Rossi Doria) and have been found with special frequency in the history of women with certain types of new growth, notably carcinoma of the fundus (Mayer)

The average age of puberty in these women with tumors of the breast is shown in table 8 to be approximately 14 years, which corresponds almost exactly with the normal for American girls as determined by Engelmann, although it is somewhat lower than the average age for the European countries in which many of the women were born (Schaeffer, Schiöder) If, however, one regards as slightly abnormal a puberty that occurs before the thirteenth or after the sixteenth year, one finds such deviations from the normal slightly more often among patients with fibro-adenoma and among young patients with cancer than in the other tumor groups

(B) *The Periodicity of Menstruation*—The chronologic rhythm of the menstrual flow supplies a pure index of ovarian function, for the time of the periods is determined entirely by ovulation According to Schroder, a short cycle is to be explained on the basis of an early death of the ovum and as such is probably not productive of permanent hyperplastic changes in the epithelium of the breast unless a too rapid recurrence of the stimulative phase could produce such effects A long interval may on the other hand be the result of a persistent follicle the supposed cause of hyperplastic endometritis or the result of a persistent corpus luteum which has also been reported as the cause of a marked degree of endometrial hypertrophy (Curtis) To link these facts to those of the pathology of the breast there is the similarity between the causes of physiologic activity in breast and endometrium and also certain histologic evidence offered by Dieckmann's observation of pathologic proliferation in the breasts of women suffering from amenorrhea of long standing

A brief explanation of the methods used in compiling tables 9 A and B is necessary The types of period were classed as four week periods if the cycle was of not less than twenty-six or more than thirty-one days and also if greater deviations were of only occasional occurrence Thus the group regarded as normal contains some women with minor irregularities and the groups of women reported as having periods recurring at three to four or four to five week intervals comprises only cases with definite deviations from the normal The groups listed under three weeks and under five weeks include also some women who were menstruating every two weeks and some every six to twelve weeks respectively

Although the chief conclusions are to be drawn from the comparison of relative incidence of menstrual irregularities in the various pathologic and age groups of this series, it is perhaps useful for the purpose

TABLE 8—Age of Puberty

	Premenopause					Menopause					Postmenopause				Total					
	Total Cases	Average Age	% Normal	% Early	% Late	Total Cases	Average Age	% Normal	% Early	% Late	Total Cases	Average Age	% Normal	% Early	% Late	Total Cases	Average Age	% Normal	% Early	% Late
Fibroadenoma	20	13.5	15	35	20	3	(15.5)	(23)	0	(27)	1	(18.0)	0	0	(100)	21	11.0	12	27	62
Painful nodules	18	11.0	83	11	6	1	(11.0)	(100)	0	0	0					19	11.0	81	11	5
Chronic cystitis	23	13.5	83	8	8	21	14.0	57	11	29	3	(14.5)	(100)	0	0	17	11.0	72	11	17
Papillary growths	5	(15.0)	(20)	(20)	(60)	3	(15.5)	(33)	0	(67)	1	(13.0)	(100)	0	0	9	15.0	11	33	55
Total benign	66	13.8	67	19	13	28	11.5	53	11	36	5	11.8	(80)	0	(20)	46	14.1	61	15	21
Total malignant	11	11.0	62	23	15	57	14.0	60	19	21	15	14.2	60	20	20	136	11.1	60	21	19

Explanation—Normal puberty at 13, 14 or 15 years

of general orientation to note that from the examination of the statistics of several writers (Krieger, Kelly, Hart and Barbour, Webster), it appears that a minimum of 75 per cent of all women have a twenty-six to thirty day cycle, while some writers have placed the figure as high as 95 per cent

The tables dealing with menstrual frequency (9 *A* and *B*) contain material which in its implications is the most important in the paper. A few special points must be made

1 The original or "constitutional" pattern of menstruation is perhaps as often normal among women with chronic mastitis and with carcinoma at all ages as it is for women in general, but a larger percentage of the women with fibro-adenomas and "painful nodules" have suffered from irregular types of menstruation since puberty (table 9 *A*)

2 The frequency of original abnormalities shows a steady decrease with the increase in the age of tumor incidence, which is perhaps due to the displacement of congenital anomalies as exciting agents by other forms of ovarian disorder

3 Turning to a consideration of the type of menstruation being experienced by the patients at the time of the onset of the tumor, one finds a great increase in the percentage of women with abnormal periodicity. This increase affects practically all of the pathologic groups and it is striking that the occurrence of these irregular types is almost as common in the young women as it is in those over 40 in whom a greater frequency should be looked for on account of the nearness of the menopause

4 It is possibly significant that among the major types of menstrual anomaly, it is particularly the increased interval variety that shows the gain. This tendency toward a longer cycle is particularly marked among the malignant cases

5 Of the women who were still menstruating when the tumor appeared, 33 per cent with benign and 32 per cent with malignant growths had experienced an alteration in the length of the interval (table 11 *A*). That most of the new types of menstruation have appeared within a short time before the appearance of the breast tumor is shown in table 12

(*C*) *The Volume and Duration of Menstruation*—The number of days of flow and the quantity of blood lost bear a less direct relationship to the ovarian function than does the periodicity just discussed. Particularly is increased duration or strength of flow rarely a true measure of ovarian function but is more indicative of a local pathologic process in the pelvis such as inflammations, congestions, tumors and displacements. Diminished bleeding, on the other hand, may as a rule be regarded as a sign of ovarian insufficiency. These principles are to be applied in the interpretation of tables 10 *A* and *B*

TABLE 9—A Original Types of Menstrual Cycle

	Premenopause				Menopause				Postmenopause				Totals			
	Available Cases	Total 1 Weeks	Per Cent 4 Weeks	3 Weeks or Less	5 Weeks or More	Per Cent 4 Weeks	3 Weeks or Less	5 Weeks or More	Per Cent 4 Weeks	3 Weeks or Less	5 Weeks or More	Per Cent 4 Weeks	Available Cases	Total 4 Weeks	Per Cent 4 Weeks	3 Weeks or Less
Fibroid adenomas	11	31	76	3	1	63	59	0	1	0	0	100	155	138	89	1
Painful nodules	21	71	25	1	1	52	41	0	0	0	0	100	116	78	67	1
Chronic cystitis	10	27	63	0	0	19	0	0	1	0	0	100	57	6	55	1
Papillary growths	6	2	33	2	1	33	24	4	1	0	0	100	11	10	83	1
Total benign	78	19	63	6	9	65	59	0	0	0	0	100	96	15	89	3
Malignant	11	31	76	3	1	63	59	0	1	0	0	100	155	138	89	1

B Types of Menstrual Cycle at Time of Onset of Tumor

	Premenopause				Menopause (Exclusive of B <sub>3</sub> )				Totals			
	Available Cases	Total 1 Weeks	Per Cent 4 Weeks	3 Weeks or Less	5 Weeks or More	Per Cent 4 Weeks	3 Weeks or Less	5 Weeks or More	Available Cases	Total 1 Weeks	Per Cent 4 Weeks	3 Weeks or Less
Fibroid adenomas	11	23	56	5	6	19	22	1	81	45	51	8
Painful nodules	21	39	50	5	13	18	13	3	104	52	50	14
Chronic cystitis	30	19	63	1	27	53	27	1	9	2	22	4
Papillary growths	6	1	17	1	3	33	11	0	24	13	37	3
Total benign	78	39	50	11	27	18	13	1	104	52	50	14
Malignant	11	23	56	5	6	19	22	1	81	45	51	8

Since the amount and the duration of flow bear almost the same significance and since the patient's reports of amounts are difficult to analyze, the study will be limited to the question of the number of days of flow except in the consideration of changes in menstruation when the patient's report of changes in volume (as opposed to actual volume) appears to be reliable

As regards the usual monthly duration of menstruation, it may be said that any length of flow within the range of from three to six days cannot be considered abnormal. In 500 cases in private practice, Bland reported that 77.8 per cent of the women had periods lasting from three to six days, 15.4 per cent for a longer and 6.8 per cent for a shorter time. In 4,542 cases, Mayer found 6 per cent with from one to two day periods and 28.8 per cent with from seven to eight day periods.

From a study of table 10 *B*, the following is to be noted

1 The original duration of the menses is practically the same in each tumor group as it is for women in general

2 When the duration of the menses as present at the time of onset of the tumor is studied (table 10 *B*), it is found that there is a small but definite increase in the percentage of cases with an abnormally short flow. This frequency of a short type of menstruation is found most often in relation to cases of carcinoma and of chronic mastitis. Particularly in the group of malignant tumors it is noticeable that a decrease in the amount or duration of bleeding is found almost as often in the young group of women as it is in those of the menopausal ages.

3 In regard to the changes in amount or duration of the menses of the individual patients (table 11 *B*), it is found that such changes had occurred in 46 per cent of all benign and 41 per cent of all malignant cases. These changes were usually of the nature of a decrease in amount and duration of flow. That most of these changes occurred in close proximity to the time of the incidence of the tumor is shown in table 12.

*Summary*—A study of the subject of a menstrual change of some type, i. e., either of frequency, duration or volume of menses or any combination of these, as outlined in table 11 *C*, indicates that well over a half of the women, who were still menstruating at the time of the onset of the tumor, had noted a recent change in the characteristics of their menstruation indicating some minor or major variation in the ovarian effect on the endometrium. Yet an empirically determined association of menstrual irregularities might perhaps have little claim to serious consideration, were there not reasons for believing that certain of these changes might be expected to produce proliferative processes in the breast.

TABLE 10—A Original Duration of Menstrual Periods

	Premenopause					Menopause					Postmenopause					Total						
	Available Cases	Total 3-6 Days	Per Cent 3-6 Days	1-2 Days	3-4 Days	5-6 Days	7 Days and Over	Available Cases	Total 3-6 Days	Per Cent 3-6 Days	1-2 Days	3-4 Days	5-6 Days	7 Days and Over	Available Cases	Total 3-6 Days	Per Cent 3-6 Days	1-2 Days	3-4 Days	5-6 Days	7 Days and Over	
Fibroid adenomas	11	33	80	5	23	10	3	61	18	75	4	32	16	12	19	41	84	4	28	13	1	
Pituitary growths	78	67	96	3	36	31	8	33	26	80	3	19	7	1	1	5	116	98	81	39	12	
Chronic mastitis	30	28	63	1	19	10	2	24	18	75	3	13	5	0	1	3	57	49	86	16	1	
Papillary growths	6	1	67	0	1	1	1	1	1	100	0	0	0	0	0	1	11	6	5	1	1	
Total benign	121	129	86	9	63	52	14	106	63	75	10	64	28	13	22	122	122	79	59	63	19	
Malignant	11	33	80	5	23	10	3	61	18	75	4	32	16	12	19	41	84	4	28	13	1	

B Duration of Menstrual Periods at Time of Onset of Tumor

	Premenopause					Menopause (Exclusive of B <sub>3</sub> )					Total				
	Available Cases	Total 3-6 Days	Per Cent 3-6 Days	1-2 Days	3-4 Days	5-6 Days	7 Days and Over	Available Cases	Total 3-6 Days	Per Cent 3-6 Days	1-2 Days	3-4 Days	5-6 Days	7 Days and Over	
Fibroadenomas	83	86	77	8	12	7	2	82	83	75	15	37	16	10	
Pituitary nodules	84	89	77	11	12	7	2	101	88	77	15	37	16	10	
Chronic mastitis	30	27	50	9	11	6	3	6	29	71	10	22	13	2	
Papillary tumors	9	1	68	1	0	0	0	6	9	68	1	0	6	2	
Total benign	127	123	77	20	25	13	5	104	121	75	15	74	36	12	
Malignant	12	91	72	7	13	6	3	12	81	68	12	28	11	3	



TABLE 11—*A Changes in Periodicity of Menstruation*

	Premenopause						Menopause (Exclusive of B.)						Totals					
	Available Cases		Total With Change in Periodicity	Per Cent With Change in Periodicity	Increased Pre- quency (Shorter Cycles)	Decreased Fre- quency (Longer Cycles)	Available Cases		Total With Change in Periodicity	Per Cent With Change in Periodicity	Increased Pre- quency	Decreased Fre- quency	Available Cases		Total With Change in Periodicity	Per Cent With Change in Periodicity	Increased Pre- quency	Decreased Fre- quency
Fibroid adenomas	21	3	14	1	1	2	43	0	0	(100)	0	0	24	9	12	32	8	19
Painful nodules	21	8	38	5	3	3	3	1	1		0	1	22	9	41	5	4	
Chronic mastitis	30	9	39	7	2	2	20	10	10	50	7	3	50	19	38	14	5	
Cystic degeneration	6	3	9	3	0	0	3	1	1	(33)	0	1	9	4	41	3	1	
Vaginitis	78	23	101	16	7	7	27	12	12	44	7	5	105	35	33	23	12	
Malignant	41	10	51	4	6	6	43	17	17	40	4	13	84	27	32	8	19	

### B Changes in Volume and Duration of Menstruation

	Premenopause				Menopause (Exclusive of B <sub>2</sub> )				Totals			
	Duration		Volume		Duration		Volume		Duration		Volume	
1 Fibro-adenomas	11	15	1	13	33	0	1	15	18	13	23	1
2 Painful nodules	6	17	1	24	100	0	1	1	22	10	32	1
3 Chronic mastitis	30	13	1	11	17	6	7	13	50	30	80	5
4 Papillary tumors	75	17	1	21	67	0	1	0	9	16	25	1
5 Total benign	11	15	1	13	221	6	10	16	107	48	155	8
6 Malignant	11	15	1	13	11	1	9	13	31	18	49	5
7 Total	22	30	2	26	33	0	1	1	138	66	204	13
8 Available Cases	12	19	1	13	1	1	1	1	12	4	17	2
9 Per Cent With	12	19	1	13	100	0	1	1	22	10	32	1
10 Change in Volume	12	19	1	13	17	6	7	13	50	30	80	5
11 or Duration	12	19	1	13	67	0	1	0	9	16	25	1
12 Total	22	30	2	26	221	6	10	16	107	48	155	8
13 Available Cases	12	19	1	13	11	1	9	13	31	18	49	5
14 Per Cent With	12	19	1	13	33	0	1	1	138	66	204	13
15 Change in Volume	12	19	1	13	100	0	1	1	22	10	32	1
16 or Duration	12	19	1	13	17	6	7	13	50	30	80	5
17 Total	22	30	2	26	67	0	1	0	9	16	25	1
18 Available Cases	12	19	1	13	221	6	10	16	107	48	155	8
19 Per Cent With	12	19	1	13	11	1	9	13	31	18	49	5
20 Change in Volume	12	19	1	13	33	0	1	1	138	66	204	13
21 or Duration	12	19	1	13	100	0	1	1	22	10	32	1
22 Total	22	30	2	26	17	6	7	13	50	30	80	5
23 Available Cases	12	19	1	13	67	0	1	0	9	16	25	1
24 Per Cent With	12	19	1	13	221	6	10	16	107	48	155	8
25 Change in Volume	12	19	1	13	11	1	9	13	31	18	49	5
26 or Duration	12	19	1	13	33	0	1	1	138	66	204	13
27 Total	22	30	2	26	100	0	1	1	22	10	32	1
28 Available Cases	12	19	1	13	17	6	7	13	50	30	80	5
29 Per Cent With	12	19	1	13	67	0	1	0	9	16	25	1
30 Change in Volume	12	19	1	13	221	6	10	16	107	48	155	8
31 or Duration	12	19	1	13	11	1	9	13	31	18	49	5
32 Total	22	30	2	26	33	0	1	1	138	66	204	13
33 Available Cases	12	19	1	13	100	0	1	1	22	10	32	1
34 Per Cent With	12	19	1	13	17	6	7	13	50	30	80	5
35 Change in Volume	12	19	1	13	67	0	1	0	9	16	25	1
36 or Duration	12	19	1	13	221	6	10	16	107	48	155	8
37 Total	22	30	2	26	11	1	9	13	31	18	49	5
38 Available Cases	12	19	1	13	33	0	1	1	138	66	204	13
39 Per Cent With	12	19	1	13	100	0	1	1	22	10	32	1
40 Change in Volume	12	19	1	13	17	6	7	13	50	30	80	5
41 or Duration	12	19	1	13	67	0	1	0	9	16	25	1
42 Total	22	30	2	26	221	6	10	16	107	48	155	8
43 Available Cases	12	19	1	13	11	1	9	13	31	18	49	5
44 Per Cent With	12	19	1	13	33	0	1	1	138	66	204	13
45 Change in Volume	12	19	1	13	100	0	1	1	22	10	32	1
46 or Duration	12	19	1	13	17	6	7	13	50	30	80	5
47 Total	22	30	2	26	67	0	1	0	9	16	25	1
48 Available Cases	12	19	1	13	221	6	10	16	107	48	155	8
49 Per Cent With	12	19	1	13	11	1	9	13	31	18	49	5
50 Change in Volume	12	19	1	13	33	0	1	1	138	66	204	13
51 or Duration	12	19	1	13	100	0	1	1	22	10	32	1
52 Total	22	30	2	26	17	6	7	13	50	30	80	5
53 Available Cases	12	19	1	13	67	0	1	0	9	16	25	1
54 Per Cent With	12	19	1	13	221	6	10	16	107	48	155	8
55 Change in Volume	12	19	1	13	11	1	9	13	31	18	49	5
56 or Duration	12	19	1	13	33	0	1	1	138	66	204	13
57 Total	22	30	2	26	100	0	1	1	22	10	32	1
58 Available Cases	12	19	1	13	17	6	7	13	50	30	80	5
59 Per Cent With	12	19	1	13	67	0	1	0	9	16	25	1
60 Change in Volume	12	19	1	13	221	6	10	16	107	48	155	8
61 or Duration	12	19	1	13	11	1	9	13	31	18	49	5
62 Total	22	30	2	26	33	0	1	1	138	66	204	13
63 Available Cases	12	19	1	13	100	0	1	1	22	10	32	1
64 Per Cent With	12	19	1	13	17	6	7	13	50	30	80	5
65 Change in Volume	12	19	1	13	67	0	1	0	9	16	25	1
66 or Duration	12	19	1	13	221	6	10	16	107	48	155	8
67 Total	22	30	2	26	11	1	9	13	31	18	49	5
68 Available Cases	12	19	1	13	33	0	1	1	138	66	204	13
69 Per Cent With	12	19	1	13	100	0	1	1	22	10	32	1
70 Change in Volume	12	19	1	13	17	6	7	13	50	30	80	5
71 or Duration	12	19	1	13	67	0	1	0	9	16	25	1
72 Total	22	30	2	26	221	6	10	16	107	48	155	8
73 Available Cases	12	19	1	13	11	1	9	13	31	18	49	5
74 Per Cent With	12	19	1	13	33	0	1	1	138	66	204	13
75 Change in Volume	12	19	1	13	100	0	1	1	22	10	32	1
76 or Duration	12	19	1	13	17	6	7	13	50	30	80	5
77 Total	22	30	2	26	67	0	1	0	9	16	25	1
78 Available Cases	12	19	1	13	221	6	10	16	107	48	155	8
79 Per Cent With	12	19	1	13	11	1	9	13	31	18	49	5
80 Change in Volume	12	19	1	13	33	0	1	1	138	66	204	13
81 or Duration	12	19	1	13	100	0	1	1	22	10	32	1
82 Total	22	30	2	26	17	6	7	13	50	30	80	5
83 Available Cases	12	19	1	13	67	0	1	0	9	16	25	1
84 Per Cent With	12	19	1	13	221	6	10	16	107	48	155	8
85 Change in Volume	12	19	1	13	11	1	9	13	31	18	49	5
86 or Duration	12	19	1	13	33	0	1	1	138	66	204	13
87 Total	22	30	2	26	100	0	1	1	22	10	32	1
88 Available Cases	12	19	1	13	17	6	7	13	50	30	80	5
89 Per Cent With	12	19	1	13	67	0	1	0	9	16	25	1
90 Change in Volume	12	19	1	13	221	6	10	16	107	48	155	8
91 or Duration	12	19	1	13	11	1	9	13	31	18	49	5
92 Total	22	30	2	26	33	0	1	1	138	66	204	13
93 Available Cases	12	19	1	13	100	0	1	1	22	10	32	1
94 Per Cent With	12	19	1	13	17	6	7	13	50	30	80	5
95 Change in Volume	12	19	1	13	67	0	1	0	9	16	25	1
96 or Duration	12	19	1	13	221	6	10	16	107	48	155	8
97 Total	22	30	2	26	11	1	9	13	31	18	49	5
98 Available Cases	12	19	1	13	33	0	1	1	138	66	204	13
99 Per Cent With	12	19	1	13	100	0	1	1	22	10	32	1
100 Change in Volume	12	19	1	13	17	6	7	13	50	30	80	5
101 or Duration	12	19	1	13	67	0	1	0	9	16	25	1
102 Total	22	30	2	26	221	6	10	16	107	48	155	8
103 Available Cases	12	19	1	13	11	1	9	13	31	18	49	5
104 Per Cent With	12	19	1	13	33	0	1	1	138	66	204	13
105 Change in Volume	12	19	1	13	100	0	1	1	22	10	32	1
106 or Duration	12	19	1	13	17	6	7	13	50	30	80	5
107 Total	22	30	2	26	67	0	1	0	9	16	25	1
108 Available Cases	12	19	1	13	221	6	10	16	107	48	155	8
109 Per Cent With	12	19	1	13	11	1	9	13	31	18	49	5
110 Change in Volume	12	19	1	13	33	0	1	1	138	66	204	13
111 or Duration	12	19	1	13	100	0	1	1	22	10	32	1
112 Total	22	30	2	26	17	6	7	13	50	30	80	5
113 Available Cases	12	19	1	13	67	0	1	0	9	16	25	1
114 Per Cent With	12	19	1	13	221	6	10	16	107	48	155	8
115 Change in Volume	12	19	1	13	11	1	9	13	31	18	49	5
116 or Duration	12	19	1	13	33	0	1	1	138	66	204	13
117 Total	22	30	2	26	100	0	1	1	22	10	32	1
118 Available Cases	12	19	1	13	17	6	7	13	50	30	80	5
119 Per Cent With	12	19	1	13	67	0	1	0	9	16	25	1
120 Change in Volume	12	19	1	13	221	6	10	16	107	48	155	8
121 or Duration	12	19	1	13	11	1	9	13	31	18	49	5
122 Total	22	30	2	26	33	0	1	1	138	66	204	13
123 Available Cases	12	19	1	13	100	0	1	1	22	10	32	1
124 Per Cent With	12	19	1	13	17	6	7	13	50	30	80	5
125 Change in Volume	12	19	1	13	67	0	1	0	9	16	25	1
126 or Duration	12	19	1	13	221	6	10	16	107	48	155	8
127 Total	22	30	2	26	11	1	9	13	31	18	49	5
128 Available Cases	12	19	1	13	33	0	1	1	138	66	204	13
129 Per Cent With	12	19	1	13	100	0	1	1	22	10	32	1
130 Change in Volume	12	19	1	13	17	6	7	13	50	30	80	5
131 or Duration	12	19	1	13	67							

(D) *Dysmenorrhea*—Dysmenorrhea in the present study refers only to the primary type which is nearly always evidence of a minor anatomic malformation (Joachimovits). It is from the point of view of this associated underdevelopment that this symptom is being studied. An approximate idea of the general frequency of dysmenorrhea may be obtained from recent studies of Sturgis and van Duyne which indicate that from 0.3 to 7 per cent of women have severe pain and from 15 to 30 per cent moderate discomfort at their periods.

TABLE 11 C—*Change in Menstruation of Some Type*

	Puberty to 35 A <sub>1</sub>			35 to 40 A <sub>2</sub>			40 to Menopause B <sub>1</sub>			Menopause B <sub>2</sub>			Total		
	Available Cases	Cases With Menstrual Change	Per Cent With Change	Available Cases	Cases With Menstrual Change	Per Cent With Change	Available Cases	Cases With Menstrual Change	Per Cent With Change	Available Cases	Cases With Menstrual Change	Per Cent With Change	Available Cases	Cases With Menstrual Change	Per Cent With Change
Fibro-adenomas	18	4	22	3	2	(66)	2	0	0	1	1	100	24	7	29
Painful nodules	20	10	50	1	1	(100)	0	0	0	1	1	100	22	12	54
Chronic mastitis	22	13	59	8	5	(63)	3	0	0	17	17	100	50	35	70
Papillary tumors	2	0	0	4	4	(100)	0	0	0	3	3	100	9	7	78
Total benign	62	27	44	16	12	75	5	0	0	22	22	100	105	61	58
Malignant	17	9	53	24	9	38	18	0	0	25	25	100	84	43	51

TABLE 12—*Elapsed Time Between Alteration in Menses and Onset of Tumor*

	Benign					Malignant				
	Exact Time Not Stated	0-23 Months	2-1 1/2 Years	5-10 Years	Total	Exact Time Not Stated	0-23 Months	2-1 1/2 Years	5-10 Years	Total
Periodicity Change	3	18	9	5	35	0	21	3	3	27
Duration Change	1	12	7	4	24	12	14	12	4	42
Volume Change	12	13	9	4	38	12	21	4	4	41

Note.—To the women of table 12 there could be added the women of class B<sub>3</sub> (benign 6 malignant 22) who had had the changes of the menopause from six months to five years before the apparent onset of the tumor and the women of C<sub>1</sub> (benign 3, malignant 24) who had had these changes from five to ten years previously.

In table 13 A, showing original frequency of dysmenorrhea and by implication the frequency of moderate maldevelopment it is clear that the fibro-adenomas again depart markedly from the average while the other groups except for the carcinomas of the early years do not vary from the ranges of van Duyne and Sturgis. Table 13 B illustrating the frequency of dysmenorrhea at the time of onset of the tumor, shows that the supposed maldevelopment has to a considerable extent disappeared in the cases of early malignancy but has persisted for the fibro-adenomas. The fact that the majority of the women with fibro-

TABLE 13—A Incidence of Dysmenorrhea During Early Life

	Premenopause					Menopause					Postmenopause					Totals				
	Available Cases					Available Cases					Available Cases					Available Cases				
	Women with- out Pain	Per Cent With- out Pain	Moderate Pain	Severe Pain		Women with- out Pain	Per Cent With- out Pain	Moderate Pain	Severe Pain		Women with- out Pain	Per Cent With- out Pain	Moderate Pain	Severe Pain		Women with- out Pain	Per Cent With- out Pain	Moderate Pain	Severe Pain	
Fibro-adenomas	21	7	33	9		4	(25)	2	1		1	1	0	0		26	9	35	7	10
Painful nodules	21	11	52	5		1	(100)	0	0		0	0	0	0		22	12	54	5	5
Chronic mastitis	30	21	70	7		21	63	7	2		3	2	(67)	0		57	38	67	14	5
Papillary tumors	6	2	30	3		4	(50)	2	0		1	0	0	0		11	4	36	5	2
Total benign	78	41	53	20		33	58	11	3		5	3	(60)	0		116	63	54	31	22
Malignant	40	15	38	17		64	59	20	9		49	28	57	18		153	81	53	55	17

B Incidence of Dysmenorrhea at Time of Onset of Tumor

	Premenopause					Menopause					Totals				
	Available Cases					Available Cases					Available Cases				
	Women with- out Pain	Per Cent With- out Pain	Moderate Pain	Severe Pain		Women with- out Pain	Per Cent With- out Pain	Moderate Pain	Severe Pain		Women with- out Pain	Per Cent With- out Pain	Moderate Pain	Severe Pain	
Fibro-adenomas	21	9	28	7		3	(33)	1	1		24	7	29	8	
Painful nodules	21	12	57	6		1	(100)	0	0		22	13	59	6	
Chronic mastitis	30	18	60	9		20	70	5	1		50	32	64	14	
Papillary tumors	6	3	50	2		3	(100)	0	0		9	6	66	2	
Total benign	78	19	50	21		27	70	6	0		105	58	30	2	
Malignant	40	22	56	11		12	67	12	2		81	50	62	26	

adenomas suffered not only pain but severe pain is corroborative evidence that fibro-adenomas occur chiefly in relatively undeveloped women

(E) *Premenstrual Breast Symptoms*—The significance of premenstrual pain and swelling in relation to hyperplasia of the epithelium and the association of these symptoms with pelvic disorders have been discussed. As the characteristics of these painful breast symptoms are not very well known, however, the following case history is cited as a fair though perhaps unusually clearcut example

R. F., aged 31, was married six and a half years before examination and widowed four years before. During her only pregnancy, which ended in a miscarriage at three and a half months, she suffered from excessive vomiting and severe breast pain. The menses had been regular since marriage but irregular previously. Eight months before admission the patient received an injury in the left breast which caused a small red spot. Six weeks later, having had in the meantime no breast symptoms, she was seized with a severe attack of nausea and vomiting, and her left breast became diffusely enlarged and tender. She was confined in bed for a week. During succeeding months the breast improved but was still tender, especially in the premenstruum. The opposite breast also became somewhat painful. Examination revealed a slender, nervous, weeping, blonde woman. Both breasts were medium-sized but erect, with firm nodular centers and normal nipples and areolae. In the outer upper quadrant of the left breast there was an ill defined lump 6 cm in diameter, exquisitely tender. The right breast was similar, a trifle smaller and also with a tender lumpiness in the outer part. The thyroid was definitely enlarged. Pelvic examination disclosed a small, conical cervix, a small, anteverted uterus tipped to the left and an enlarged, slightly tender, probably "cystic" left ovary. During two months of observation the patient has improved somewhat under a prescription of corpus luteum taken during ten days preceding menstruation and with the use of a breast support.

The study of menstrual breast symptoms (tables 14 A and B) reveals that a certain number of women particularly those in whom tumors developed at an early age, had suffered from breast pain before their periods since puberty. For many of the women, however, these premenstrual symptoms were of recent origin (table 15 A), a fact rather surprising since increasing age and marriage appear as a rule to alleviate these complaints. The close relation between the time of onset of these symptoms and the discovery of the tumor is of great importance if one accepts the view that breast pain before the periods is dependent on excessive corpus luteum stimulation.

(F) *Theoretical Anomalies of Pregnancy and Lactation*—Beside the irregular ovarian activity discussed under menstruation, there must also be considered the possibility of abnormal stimuli to the breast during gestation and lactation.

The occurrence of cancer of the breast of a peculiarly malignant variety is often observed during pregnancy. That the pregnancy is actually an important factor in initiating growth is indicated by the

TABLE 14—A Incidence of Premenstrual Breast Symptoms in Early Life

	Premenopause					Menopause					Postmenopause					Totals					
	Available Cases	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Symptoms	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Symptoms	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Pain	Women With Swelling	Available Cases	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Pain	Women With Swelling	Available Cases	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Pain	Women With Swelling
Fibro adenomas	21	9	43	9	3	(75)	1	1	(100)	0	0	1	1	(100)	0	0	26	13	50	10	10
Painful nodules	21	13	62	8	1	(100)	0	0		0	0	0	0		0	0	22	14	61	8	6
Chronic mastitis	30	13	43	9	13	75	5	1	(100)	0	0	3	3	(100)	0	0	57	34	60	11	11
Papillary tumors	6	3	50	2	4	(100)	0	0		0	0	1	1	(100)	0	0	11	8	73	2	2
Total benign	78	38	49	28	33	79	6	1	(100)	0	0	5	5	100	0	0	116	69	60	31	32
Malignant	11	19	46	15	65	63	16	16		4	2	49	14	89	4	2	155	101	67	35	35

B Incidence of Premenstrual Breast Symptoms at Time of Onset of Tumor

	Premenopause					Menopause					Totals				
	Available Cases	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Pain	Women With Swelling	Available Cases	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Pain	Women With Swelling	Available Cases	Women With- out Breast Symptoms	Per Cent With- out Breast Symptoms	Women With Pain	Women With Swelling
Fibroadenomas	16	8	50	13	11	43	25	58	13	11	42	43	52	26	22
Painful nodules	16	13	81	1	1	3	2	(67)	1	1	24	9	38	12	11
Chronic mastitis	30	13	43	13	11	20	14	70	3	1	50	27	54	16	17
Papillary tumors	6	1	17	1	2	3	3	(100)	0	0	9	4	44	1	4
Total benign	78	21	27	49	36	27	19	70	5	6	105	40	38	51	45
Malignant	11	13	16	13	11	43	25	58	13	11	42	43	52	26	22

Fibroadenomas  
Painful nodules  
Chronic mastitis  
Papillary tumors  
Total benign  
Malignant

reports of development of cancer during gestation in a single breast after the previous removal of the other for carcinoma Trout observed this happening in the later history of two of his own cases and in reply to his inquiries sent to other physicians learned of thirteen similar instances

Development of cancer during lactation may be attributable to the increase in size of microscopic cancer seeds formed during the

TABLE 15—1 *Changes in Severity of Dysmenorrhea and Breast Symptoms Before Onset of Tumor*

	Premenopause						Menopause Exclusive of B <sub>2</sub>						Totals					
	Dysmenor- rhea			Breast Symptoms			Dysmenor- rhea			Breast Symptoms			Dysmenor- rhea			Breast Symptoms		
	Avail- able Cases	Increase	Decrease	Avail- able Cases	Increase	Decrease	Avail- able Cases	Increase	Decrease	Avail- able Cases	Increase	Decrease	Avail- able Cases	Increase	Decrease	Avail- able Cases	Increase	Decrease
Fibroadenomas	21	2	2	21	2	0	3	0	0	3	0	0	24	2	2	24	2	0
Painful nodules	21	1	5	21	15	0	1	0	0	1	1	0	22	1	5	22	16	0
Chronic mastitis	30	4	1	30	12	0	20	2	3	20	3	1	50	6	4	50	15	1
Papillary tumors	6	1	1	6	2	0	3	0	1	3	0	0	9	1	2	9	2	0
Benign total	78	8	9	79	31	0	27	2	4	27	4	1	105	10	13	105	35	2
Malignant	39	0	9	39	5	4	42	1	7	43	5	1	81	1	16	82	10	5

B *Elapsed Time Between Change in Premenstrual Breast Symptoms and Onset of Tumor*

	Benign						Malignant					
	Lact Time Not Noted	0-23 Months	2 1/2 Years	5-10 Years	Over 10 Years	Total	Lact Time Not Noted	0-23 Months	2 1/2 Years	5-10 Years	Over 10 Years	Total
Increase or new appearance	0	21	10	3	1	35	0	7	1	2	0	10
Decrease or disappearance	0	0	0	0	1	1	1	3	0	1	0	5

preceding pregnancy, but it is also possible that the irregular ovulation of the lactation period may furnish the basis for atypical cell proliferation during this time Attempts to study the relation of the time of the return of the menses after parturition to the etiology of tumors were made on a small group of cases but no progress was made and this subject must be left in this very theoretical state

Kilgore has reported that 45 per cent of all cancers of the breast arise during pregnancy or lactation and of the cancers occurring under the age of 47, 10 per cent arise under these conditions So far as the present series of cases of cancer is concerned, the following relation to

pregnancy was noted Of the twenty-eight women under the age of 40 who had borne children, a lump was first noted during pregnancy in two, during lactation in three, between one and two years after a delivery in three, between two and three years in one, between three and four years in three Altogether, sixteen of the twenty-eight women (57 per cent) developed their tumor before the end of the fifth year after a delivery

(G) *The Menopause*—Lane-Claypon, by comparing the incidence of mammary cancer for any given age with the total number of women in the general population of the same age, has shown that there is probably a constant increase of susceptibility to the disease with advancing years The proof of this relationship must end the argument about the immediate effect of the menopause on the production of cancer, yet the

TABLE 16—A *Average Age of Menopause*

	B <sub>2</sub> Menopause Incomplete		B <sub>1</sub> 6 Months-5 Yrs After Cessation		C <sub>1</sub> 5-10 Years After Cessation		C <sub>2</sub> Over 10 Years After Cessation		Total	
	Available Cases		Available Cases		Available Cases		Available Cases		Available Cases	
	Average Age		Average Age		Average Age		Average Age		Average Age	
Fibro-adenomas	1	48	1	42	0		1	42	3	44
Painful nodules	1	50	0		0		0		1	50
Chronic mastitis	17	45.7	4	44.5	2	46	1	51	24	45.7
Papillary tumors	3	43.7	1	50	1	52	0		5	47.4
Total benign	22	45.7	6	45	3	48	2	46.5	33	45.8
Malignant	25	45.4	22	48	24	47.9	25	46.6	96	46.9

Note—It must be remembered that in group B<sub>2</sub> the menopause had apparently begun but was not yet completed

possibility remains that the changes in the breast produced by the ovarian irregularities of the menopausal years may be the basis for the pre-cancerous lesions from which cancers gradually take origin over a long period It appears probable that the menopausal years are the last in which benign new growths and diffuse hyperplasia of the breast may originate, and so far as cancers are derivatives of these structures, the original basis of their growth must also date back to the years before the cessation of ovarian activity

(1) *The Age of the Menopause* The age at which the menopause occurs has perhaps a slight bearing on the strength of the ovarian function Lane-Claypon's report showed that the age of menstrual cessation and the total years of sex life were essentially the same for cancer as for normal cases In the present series (table 16 A), the average age of the menopause was approximately 47, which corresponds closely with the normal figures determined by several writers (Norris, 47.89, Mayer-Krieger, 47.03 Schaeffer 47.26)





A more important feature of the menopause than that of the age of occurrence is the character and duration of the period of irregular ovulation that precede the final cessation of menstruation. Such data could unfortunately be supplied by only a few patients.

(2) *Duration of Menopause* The total time elapsing between the first irregular period and complete cessation is usually under one year. Morris reported only 13 per cent and Tilt, 28 per cent of women whose menopausal irregularities lasted over twelve months. Among the cases of tumor in this study, the duration of the menopause appears in general to be somewhat longer and this tendency is more marked in the women who developed the disease during or soon after the climax (table 16 B). Thus in the twenty-five cases of cancer of group B<sub>2</sub>, menstrual irregularities had already been noted for over a year in 36 per cent, and in these it must be remembered that final cessation had not yet occurred. The cases are, of course, too few to make this observation more than suggestive.

(3) *Type of Menopause* In the cases of cancer by far the commonest type of menopause was that characterized by a lengthening cycle (decreasing frequency of menstruation), 52 per cent of the women with carcinoma developing after the onset of the climax showing this feature. This form of menopause, of course, is not specific for cancer, yet it is true that an increasing interval between ovulations should theoretically be productive of irregular proliferative processes in the breast and may well be one of the causes of the minor degrees of chronic mastitis that can apparently be detected clinically in practically all breasts during the years of the menopause, and with which cancer is so commonly associated.

#### ASSOCIATED PELVIC DISEASE

The frequency and character of the pelvic disorders in the histories of the present series of women are charted in table 17. Since uterine and ovarian disorders are of unequal significance, they have been separated. The occurrence of operations is also specifically noted since the previous existence of pelvic disease in these cases is particularly positive.

(A) *Uterine Disease*—The uterine conditions are certainly less important than the ovarian, and yet certain points indicated by the tabulated statistics may have some bearing and must be stressed. 1 The series of conditions listed under uterine and labeled "others" include all cases of "inflammation of the womb" in which were probably a certain number of instances of salpingo-oophoritis. 2 A history of curettage for bleeding or sterility carries with it an implication of disturbed ovarian function. 3 The high incidence of fibroids is perhaps of considerable significance in linking tumors of the breast with the

TABLE 17—History of Gynecologic Disease

	Premenopausal						Menopausal						Postmenopausal						Total					
	Uterine			Ovarian			Uterine			Ovarian			Uterine			Ovarian			Uterine			Ovarian		
	Per Cent With Previous History of Gynecologic Disease	Operations on Uterus	Fibroids	Displacements	Others	Total Ovarian	Per Cent With Previous History of Gynecologic Disease	Operations on Uterus	Fibroids	Displacements	Others	Total Ovarian	Per Cent With Previous History of Gynecologic Disease	Operations on Uterus	Fibroids	Displacements	Others	Total Ovarian	Per Cent With Previous History of Gynecologic Disease	Operations on Uterus	Fibroids	Displacements	Others	Total Ovarian
Fibroids	19	26	3	2	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Painful nodules	61	17	5	0	1	1	1	1	1	1	0	1	100	0	0	0	0	1	0	0	0	1	5	1
Chronic metritis	87	13	5	3	1	1	5	2	1	1	2	2	96	6	5	1	1	0	1	1	0	1	0	1
Leptocary tumors	1	75	1	3	1	1	1	0	0	0	0	1	100	0	0	0	0	0	0	0	0	0	0	0
Benign	62	17	6	5	1	6	11	7	11	7	11	7	33	7	5	1	1	3	2	3	1	0	1	0
Malignant	81	17	8	6	2	1	2	7	5	9	1	6	27	11	5	1	4	2	9	8	5	1	13	5

Note.—The column "others" includes Benign Uterine Inflammation of womb, cervical stenosis, 1 case; curettage for discharge, 1 case; Ovarian Oophorectomy cause unknown at 19 and 20 years, *ectopic pregnancy*, 2 cases; *ovarian cyst*, 1 case; *hemorrhage and atretic trouble*, 1 case.

Malignant Uterine Adenocarcinoma of fundus, 3 cases; hysterectomy for intestinal obstruction, 1 case; curettage for sterility, 1 case; curettage for scanty flow, 1 case.

Ovarian Ovarian cysts, 2 cases; oophorectomy for bleeding, 2 cases; ovary advised removed for pain 1 case.

neoplasms of the other glandular organs connected with the sex function, for there is already a fairly well established association between uterine fibroids and tumors of the ovary, of the endometrium and of the thyroid

As regards the endometrium, Kelly and Cullen found among a series of 1,400 myomas an associated carcinoma of the fundus in 17 per cent and an associated cervical in 13 per cent, and it must be remembered that were each association an accidental one the cervical carcinoma should have occurred from five to ten times as often. Winter, Hofmeier and several other writers have likewise drawn attention to this special association of myomas with endometrial cancer. Frankl alone denied this relationship, but the statistics on which his conclusions are based give a coincidence of myomas in cases of corpus carcinoma of only 9 per cent, a figure which appears to be surprisingly low. Mahle, for instance, reported a rate of association nearly four times as high.

The association of uterine myomas with papillary cystadenoma and cystadenocarcinoma of the ovary has been reported on by me.

Attention was drawn to the common coincidence of myomas and goiter as long ago as 1891 by H. W. Freund, and since then numerous other writers have made similar observations (Elsner, Ullmann, Aschner, Bauer, Pape). Estimates of the frequency of thyroid disease in association with myoma have varied from 28 to 100 per cent, depending apparently on the geographical location of the clinic.

The possibility exists, therefore, that the occurrence of a myoma is an indication of a special predisposition of those organs chiefly affected by the cycles of pregnancy and menstruation to form tumors, a predisposition that manifests itself most readily in the form of uterine muscular tumors, but also as new growths in various glandular organs and as an association of several tumors of different types more frequently than one would expect from a chance coincidence. The nature of such a possible relationship has been best illustrated by an article of Ballin and Moehlig in which they reported that among 100 patients consulting for goiter, 18 were found to have fibroid tumors and 4 tumors of the breast, while among 100 patients consulting for fibroid tumors 35 had also a goiter and 6 a tumor of the breast.

In the present series of mammary tumors, 16 of 233 patients who were questioned were aware of previous fibroid disease and of these all but 2 had had an operation for the condition. Examination in 66 cases added seven unsuspected myomas to the list so that the association with tumors of the breast of palpable fibroids or those requiring operation may be placed somewhere between 8 and 16 per cent. The incidence of myomas of appreciable size is therefore probably though not positively higher than for women in general.

Another observation of theoretically great significance is that cancer of the breast developed almost simultaneously with a carcinoma of the endometrium in three cases. The operations on the breast and uterus were performed at intervals of twenty-four, four and five months respectively, the operation on the breast being performed first on the first two patients and that on the uterus in the last patient. The occurrence of these types of cancer in association in such frequency does not

of course, represent the normal relationship, yet the fact of the similarity of the biology of these two forms makes one believe that their association is not entirely accidental. It is at least interesting to note that Smith and Bartlett and also Seliga and Esch have noted the occurrence of these two growths in association.

(B) *Ovarian Disease*—As compared with the uterine conditions just discussed, the detection of some form of ovarian disease is much more direct evidence that the breast has been subjected to disturbing influences. The rôle of ovarian inflammation in the production of excessive premenstrual symptoms has been already discussed. The occurrence of ovarian tumors, on the other hand, may have the same significance as that of the myomas.

In the tabulated results of the study of previous ovarian disease, there appear marked differences in the type of pelvic disorder reported by the women of different ages. Now it has been stated that neoplastic changes in the breasts of young women should require the existence of a special congenital or acquired dysfunction while those of the older women might depend merely on the irregularities of function of the menopause or on the action of the changes of senility on the remnants of hyperplastic tissue. This point receives definite support from the fact that in both the benign and the malignant series about one fifth of the women of the young and middle age groups reported some form of antecedent ovarian disease and one tenth had actually been operated on for ovarian conditions, whereas among the older women this factor practically disappears from the histories.

As elsewhere in this paper, grounds for distinguishing between the specific etiology of malignancy and tumor growth in general are lacking for there is no significant difference between the occurrence of pelvic disease in the history of the cancerous and noncancerous cases. Inflammatory disease of the ovary is a trifle more commonly associated with "painful lumps" than with any other form of new growth.

(C) *Results of Physical Examination of Pelvic Organs*—Actual examination of the uterus and ovaries of about a quarter of all the patients revealed, as was to be expected, no constant gynecologic lesion. The observations noted in table 18 do illustrate, however, the universality of minor gynecologic lesions that are often symptomless. That this common pathologic process in the reproductive tract may affect the breast through the ovary is at least conceivable.

#### ASSOCIATED THYROID DISEASE

To see the significance of thyroid enlargement for the problem of hyperplasias and tumors of the breast it is only necessary to recall that the physiologic conditions favoring thyroid enlargement are the same as those producing hypertrophy of the breast.

The incidence of thyroid enlargement in the various age and tumor groups is charted in table 19. Marked divergences between classes are very apparent. The younger women show this thyroid hypertrophy most frequently, and it is particularly in the type suffering from the so-called "painful nodule," the type with the marked menstrual irregularities, that a moderate increase in the size of the thyroid is of almost regular occurrence. The cases of carcinoma among the younger women also show a considerable though somewhat lower incidence of thyroid disease.

Some writers have contended that thyroid dysfunction is directly connected with the development of cancer. By comparing the average weights of the thyroid gland with the death rates for cancer in three different geographical regions, Bern, Munich and Kiel, Bayard was able

TABLE 18—*Summary of Results of Gynecologic Examination*

Examined	Total	Group A	Group B	Group C	
Benign	37	21	14	2	
Malignant	29	5	21	3	
Ovaries					
Benign	Enlargement or inflammation, 8 [3 in confirmation of history]				
Malignant	Enlargement or inflammation, 3 [1 in confirmation of history]				
Fundus	Fibroids, Per Cent	Displaced, Per Cent	Enlarged, Per Cent	Atrophic or Hypoplastic, Per Cent	Normal Per Cent
Benign	14	62	17	22	8
Malignant	22	35	8	22	14
Cervix	Laceration or Erosion, Per Cent	Enlarged, Per Cent	Atrophic or Hypoplastic, Per Cent	Normal, Per Cent	
Benign	60	17	27	17	
Malignant	41	10	31	26	

to point out that in general the districts with the greater average thyroid weights were associated with a higher mortality from cancer. The difference in mortality rates for cancer between Italy and Switzerland illustrates the same point. Bayard attributed the higher rate for cancer to the general hypothyroidism.

Such an hypothesis as the one just noted is not offered in the present paper, but it is suggested that an endocrine or perhaps simply ovarian disorder is capable of producing a condition in the body similar to that physiologically present at puberty, and as a result growth processes of varying degrees take place simultaneously in breast and thyroid.

#### PHYSICAL EXAMINATION OF THE BREAST

The size, shape and consistence of the breasts and also the size and position of the tumors were carefully recorded descriptively and noted in the form of a diagrammatic sketch for each case. Such material lent

TABLE 19—The Association of Thyroid Disease with Tumors of the Breast

	Premenopause						Menopause						Postmenopause						Totals					
	History			Examination			History			Examination			History			Examination			History			Examination		
	Available Cases	Total Thyroid Abnormality	Per Cent Thyroid Abnormality	Previously Noted Cases	Tumor Thyroid	Symmetrical Hypertrophy	Slight Fullness	Available Cases	Total Thyroid Abnormality	Per Cent Thyroid Abnormality	Previously Noted Cases	Tumor Thyroid	Symmetrical Hypertrophy	Slight Fullness	Available Cases	Total Thyroid Abnormality	Per Cent Thyroid Abnormality	Previously Noted Cases	Tumor Thyroid	Symmetrical Hypertrophy	Slight Fullness	Available Cases	Total Thyroid Abnormality	Per Cent Thyroid Abnormality
Fibroid adenomas	18	6	33	3	0	5	1	2	0	0	0	0	0	0	1	0	0	0	0	0	0	21	6	28
Painful nodules	18	15	83	7	0	12	2	1	1	100	0	0	0	1	0	0	0	0	0	0	0	19	16	84
Chronic mastitis	26	9	35	1	0	3	6	18	3	17	2	2	0	1	3	0	0	0	0	0	0	17	12	25
Papillary tumors	1	3	75	1	0	0	2	2	1	50	1	1	0	0	1	1	100	1	1	0	0	7	5	71
Total benign	66	33	50	12	0	20	11	23	5	22	3	3	0	2	5	1	(20)	1	1	0	0	94	39	42
Malignant	33	9	27	4	2	5	2	55	8	15	4	2	3	3	42	2	5	0	1	0	1	130	19	15

TABLE 20—Size and Shape of Breast

	Premenopause						Menopause						Postmenopause						Total						
	Size			Shape			Size			Shape			Size			Shape			Size			Shape			
	Large	Medium	Small	Pendulous	Medium	Erect	Large	Medium	Small	Pendulous	Medium	Erect	Large	Medium	Small	Pendulous	Medium	Erect	Large	Medium	Small	Pendulous	Medium	Erect	
Fibroid adenomas	21	3	7	11	52	1	4	13	62	4	0	1	3	(75)	1	0	3	(75)	1	1	0	0	0	0	0
Painful nodules	21	1	11	6	29	6	2	13	62	1	0	0	1	(100)	0	0	1	(100)	0	1	0	0	1	0	
Chronic mastitis	29	8	12	9	31	15	10	1	13	21	10	13	1	4	17	5	2	8	3	1	2	0	2	1	
Papillary tumors	6	0	3	3	50	1	1	1	(25)	2	1	1	1	(25)	1	0	0	1	0	0	1	0	0	0	
Benign	77	15	33	29	38	26	17	31	11	33	12	15	6	18	20	6	7	21	5	2	2	1	20	3	
Malignant	10	8	15	17	13	17	11	9	23	63	15	35	13	21	10	17	9	9	16	7	30	9	20	26	

itself with difficulty to statistical tabulation, but led to a few definite impressions

(A) *Size and Shape of Breast*—In general, it may be said that the small, erect breast is found in childless and relatively underdeveloped women. Large and pendulous breasts occur in the opposite type, although excessive obesity and age may tend to produce the same effect without lactation. Table 20 is confirmatory of the charts on marriage and childbirth in that it shows the fibro-adenomas occurring chiefly in the small, erect breasts and chronic mastitis in the larger and pendulous ones. The cases of "painful lump" and those of early carcinoma appear less definitely related to breast form.

(B) *Type of Nipple and Areola*—Although not charted, it may be said that the areola in the breast with fibro-adenoma is typically small and dark with a small well formed nipple. It is the virginal type approaching sometimes even the male form. In the cases of chronic mastitis the nipple is as a rule larger, the areola of much greater area, often light in color and less demarcated against the skin.

(C) *Consistence*—The consistence of the unaffected breast is also of some interest, for one gains a decided impression that the structure of the tumor is related to the architecture of the breast tissue from which it is derived. In the great majority of the women with fibro-adenoma, the breast tissue was localized in the retro-areolar region and was frequently palpable as firm, lobulated masses of a consistence not unlike that of the fibro-adenoma itself. That such lobulated and slightly isolated tissue may often be removed under the impression that it is a true tumor has been convincingly demonstrated by McFarland. In the typical cases of chronic mastitis noted in this study, the breast tissue was neither concentrated nor lobulated but disposed diffusely or in the form of small nodules throughout most of the gross extent of both breasts. In practically all cases both breasts were involved, and from the sketches it appears that the points of chief localization of the process are usually strikingly symmetrical in the two breasts.

That the presence of carcinoma in one breast implies a special susceptibility to cancer formation in the other breast as well has been fairly well proved by Kilgore, who has computed statistics to show that any woman who has survived an operation for cancer of the breast for five years has from three to four times the chance of developing cancer in the remaining breast than would the average woman. These remote developments of cancer after operation are believed by Kilgore to be properly regarded as independent growths in the great majority of the cases, and it is likely that many of the more immediate involvements of the second breast should be similarly interpreted. The entire phenomenon of the bilateral development of cancer of the breast is slight additional evidence against an entirely local cause for mammary neoplasms.

(D) *Position of the Tumor* —Particular attention in the examination of the patient was paid to the location of the tumor in the breast and especially to its relation to the nipple, since it was thought possible that different histologic forms might occur in different sections of the duct system and might even on that account have a different etiology. This attempt met with no success since it now appears probable that the actual distances from the nipple, as they were recorded, have a varying significance depending on the size and shape of the breast.

The occurrence of cancer with particular frequency in the upper outer quadrant has long evoked interest and has been explained on the supposition that drainage is most difficult and stasis most common in this region. Against this point of view may be mentioned two points. In the first place, it should be clear that in pendulous breasts the upper quadrant far surpasses all others in size and that with the nipple at the most dependent portion of the breast the lower quadrants practically disappear. But beyond this inequality of the size of the quadrants there is often clinical evidence that a greater concentration of glandular tissue exists in the tails of even normal breasts than elsewhere. Hence when cancer appears in the upper and outer quadrant, it is probable that it is merely developing in the region where the greatest number of cells are subject to the chance of malignant transformations.

#### NOTES ON GENERAL PHYSICAL CONSTITUTION

In the present study of tumors of the breast it had been hoped that anthropometric measurements could be employed such as those used so successfully by Draper, but the scope of this problem at once appeared beyond the efforts of a single worker. The records of weights and descriptive notes on certain points thought to have a special relationship to the reproductive system can therefore alone be offered.

(A) *General Body Form* —It has frequently been suggested that certain types of persons have a special predisposition to develop tumors. Rokitsansky drew attention to the antagonism between tuberculosis and cancer. Beneke, by actual measurements, concluded that cancer was a disease particularly of the broadly built, plethoric type of person. Beneke's work has been confirmed in recent years by the studies of P. Cohnheim on gastro-intestinal cancers and of Takata and Suzue on gynecologic carcinomas. Barker also has rather theoretically expressed the opinion that cancer was associated with good nutrition.

A more detailed consideration of the subject leads to certain possible reservations.

1. The constitutional type predisposed to neoplastic growth may be variable for different organs and for different forms of cancer. One would hardly expect cancer of the stomach developing on the basis of



gastric ulcer to be found chiefly in the broadly built and overnourished persons. On the other hand, there is some reported evidence that points to the association of overweight, particularly with certain of the forms of tumor that have been described, as allied to the neoplasms of the breast. Many writers, for example, have found that myomas occur especially in the well nourished (Hofmeier, Theilhaber, Pape, Beneke). Pinard noted the development of thyroid disease in association with weight increase, and Katz has made a similar observation on endometrial cancer.

2 The "cancer type" may be different for people of different ages, for Aschner wrote that cancer in the young is more apt to appear in the slender and undernourished type. Schmidt expressed the same opinion in special reference to gastro-intestinal cancer. A similar predisposition may exist for the benign growths, for Aschner likewise believes that myomas when they develop early favor slender types, with hypertichosis and genital maldevelopment.

The few observations made on the physical constitution of the women in the present group are in general consistent with the views of the writers that have just been discussed.

(1) General Body Form. Table 21, in which is charted a summary of the examiner's impression of the general proportions of the patients, shows that the fibro-adenoma series in particular contains a very high percentage of undernourished women, while among the older patients with cancer there are an extraordinary number who were strikingly large and heavy.

(2) Average Weights. In table 22 are listed the average number of pounds which the patients reported as having been their weight when the tumor was first noted and before any loss from the effects of the disease itself had occurred. For comparison with this table there is appended a chart originally compiled by Weisse, showing the average weights of a very large number of women at different age levels. The women of this control were weighed in clothes and shoes corresponding in this respect to the state of dress under which the reported weights of the women with tumors were also obtained. For further accuracy, the mean age of the women of each pathologic and physiologic age group is given to aid in picking the proper weight for comparison from the chart of normal women.

A consideration of chart 21 shows that the young women with fibro-adenomas averaged 8 pounds (3.6 Kg.) less than the normal for their age. Those with malignant cases were from 4 to 6 pounds (1.8 to 2.7 Kg.) underweight. The women with chronic mastitis were at all ages a trifle overweight. Most striking of all, however, is the fact that among the older age groups with carcinoma, the average weights run

	Premenopause										Menopause										Postmenopause										Total														
	Available Cases					Per Cent Above Normal					Per Cent Below Normal					Available Cases					Per Cent Above Normal					Per Cent Below Normal					Available Cases					Per Cent Above Normal					Per Cent Below Normal				
	Immense	Heavily Built	Normal	Slender	Thin	Thin	Per Cent Above Normal	Per Cent Below Normal	Available Cases	Immense	Heavily Built	Normal	Slender	Thin	Thin	Per Cent Above Normal	Per Cent Below Normal	Available Cases	Immense	Heavily Built	Normal	Slender	Thin	Thin	Per Cent Above Normal	Per Cent Below Normal	Available Cases	Immense	Heavily Built	Normal	Slender	Thin	Per Cent Above Normal	Per Cent Below Normal											
Fibroid adenomas	21	1	2	5	7	6	11	62	3	0	1	1	1	0	0	(33)	(33)	1	1	0	0	0	0	0	(100)	0	25	2	3	6	8	6	20	56											
Painful nodules	19	0	3	6	5	5	16	53	1	0	1	0	0	0	0	(100)	0	0	0	0	0	0	0	0	0	20	0	1	6	5	5	20	50												
Chronic mastitis	28	3	8	7	7	3	39	35	21	5	10	5	2	2	0	62	17	3	1	0	1	1	1	0	(33)	55	9	18	13	10	5	49	27												
Papillary tumors	6	0	2	2	1	1	33	33	3	0	2	0	1	0	0	(67)	(33)	1	0	0	1	0	0	0	0	10	0	4	3	2	1	40	30												
Benign tumors	71	4	15	20	20	15	26	17	31	5	14	6	4	2	61	20	5	49	12	19	12	6	0	0	63	12	149	26	59	36	23	5	57	19											
Malignant	38	1	10	13	7	4	37	29	62	10	30	11	10	1	64	18	18	19	12	19	12	6	0	0	0	63	12	149	26	59	36	23	5	57	19										

TABLE 22—Average Weights at Time of Onset of Tumor

	A <sub>1</sub> Puberty to 35					A <sub>2</sub> 35-40					B <sub>1</sub> 40-Onset of Menopause					B <sub>2</sub> Intra-menopause					B <sub>3</sub> 6 Mos -5 Yrs Postmenopause					C <sub>1</sub> 5-10 Years Postmenopause					C <sub>2</sub> Over 10 Years Postmenopause					Total														
	Available Cases					Average Age for Group					Available Cases					Average Age for Group					Available Cases					Average Age for Group					Available Cases					Average Age for Group					Available Cases					Average Age for Group				
	17	21.5	119	125	8	3	36	0	121	2	44.5	126	5	0	1	50	0	145	3	46	7	168	1	43	152	0	0	2	53	156	5	1	81	112	50	37	0	140	8											
Fibroid nodules	18	26	8	125	8	0	7	37	5	0	2	40	0	139	0	15	45	4	147	3	46	7	168	0	1	43	152	0	0	2	53	156	5	1	81	112	50	37	0	140	8									
Chronic mastitis	20	29	0	135	3	4	38	0	137	0	0	0	132	7	3	43	7	147	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
Papillary tumors	0	55	27	0	127	3	11	36	9	130	4	42	2	132	7	19	45	4	146	4	47	6	161	5	3	54	3	147	7	2	68	166	101	35	0	135	5	8	40	5	140									
Total benign	55	27	0	127	3	11	36	9	130	4	42	2	132	7	19	45	4	146	4	47	6	161	5	3	54	3	147	7	2	68	166	101	35	0	135	5	8	40	5	140										
Malignant	16	29	8	125	19	36	8	111	8	16	13	0	159	5	19	45	4	147	4	20	50	5	152	9	21	55	1	153	5	22	60	4	159	9	133	46	7	151	8	13	46	7	151							

Note—The weights are those of the patients at the time of the tumor's onset as reported by the patient herself

Table of Average Weights of Normal Women for Comparison

Age Weights	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	All Ages
	123	127	129	133	136	139	143	144	146	143	133

Note—Life Insurance statistics on 59 525 women weighed in clothes and shoes (Weisse)

from 2 to 20 pounds (0.9 to 9 Kg.) heavier than those of normal women at a corresponding age.

Were these observations corroborated, one must surely interpret them as indicating a predisposing effect of an abnormal (possible hyperthyroid) constitution in the young women with cancer of the breast and some special acquired glandular disposition in the older women that manifests itself as a tendency to excess deposit of fat. The statistics as given here are, of course, based on an exceedingly small number of cases, but some weight must be given them when it is remembered that they are in general confirmatory of previous studies on cancer in general and on uterine myoma, a tumor of the same body system as the breast.

(3) *Changes in Weight* Table 23 has been prepared to show the history of weight variations during the ten years antedating the discovery of the tumor. It appears that of the women with carcinoma belonging to the early and middle age groups, over one-third had noted a gain of more than 10 pounds (4.5 Kg.), while the older women gave this history a trifle less frequently. These gains in weight are perhaps a little different from those occurring in the normal woman, but it is possibly significant that the increase is as frequently noted in the young woman as in those of the menopause age. An exception to the general rule of increasing weight is noted among the women with fibro-adenomas who in many cases reported losses in weight.

(B) *Race and Pigmentation*—It has been asserted (Aschner) that cancer is peculiarly prevalent among dark haired and deeply pigmented persons, and furthermore, that various races have different degrees of susceptibility and immunity to certain types of tumor.

The results of observations on the color of the hair of the women in the present study (table 24) offer only one point worthy of note. The localized benign tumors show a special tendency to occur in the blonde and brown haired women and chronic mastitis and cancer in the black haired.

The racial distribution (table 25) undoubtedly accounts for this apparent tendency of persons with certain types of pigmentation to develop special forms of tumors, but whether this arrangement itself is indicative of actual racial predispositions or whether it is adventitious depending on an outside sorting of cases referred to the hospital is not clear. The peculiar predominance of Jewish women among the cases of chronic mastitis developing at the menopause and their almost complete absence from among the women with fibro-adenomas raises the question of whether functional difficulties at the climax may not be especially common in women of this race.

(C) *Hypertrichosis*—The pattern of the facial and body hair is an accepted secondary sexual characteristic and should therefore be of con-

TABLE 23—Changes in Weight During Ten Years Preceding Onset of Tumors

	Premenopause						Menopause						Postmenopause						Total					
	Gain			Loss			Gain			Loss			Gain			Loss			Gain			Loss		
	Available Cases	3-10 Lbs	11-20 Lbs	Over 20 Lbs	Per Cent Over 10 Lbs	Per Cent Over 20 Lbs	Available Cases	3-10 Lbs	11-20 Lbs	Over 20 Lbs	Per Cent Over 10 Lbs	Per Cent Over 20 Lbs	Available Cases	3-10 Lbs	11-20 Lbs	Over 20 Lbs	Per Cent Over 10 Lbs	Per Cent Over 20 Lbs	Available Cases	3-10 Lbs	11-20 Lbs	Over 20 Lbs	Per Cent Over 10 Lbs	Per Cent Over 20 Lbs
Fibroadenomas	61	2	2	1	3	1	26	1	0	1	(0)	(0)	1	0	0	0	(0)	(0)	15	3	3	9	1	62
Painful nodules	15	1	1	1	1	0	9	0	0	0	(0)	(0)	0	0	0	0	(0)	(0)	14	1	1	1	0	5
Chronic cystitis	92	3	2	2	2	0	19	5	2	1	21	(0)	2	0	2	0	(0)	(0)	21	7	8	6	3	17
Papillary tumors	1	0	0	1	1	0	23	1	0	0	(0)	(0)	1	0	0	0	(0)	(0)	8	0	0	2	25	81
Total benign	99	9	9	3	10	3	57	5	5	5	24	3	3	0	1	0	(25)	(25)	86	11	15	19	33	19
Atypical	36	1	8	3	2	0	6	11	7	11	33	2	1	1	1	0	10	10	131	22	21	22	33	7

siderable importance in any attempt to correlate function of the sex gland with neoplasms of the reproductive system Ovarian tumors have, for example, been frequently reported in association with a developing hypertrichosis (Halban), and the occurrence of myomas in young women with excessive hair has been mentioned (Aschner)

The existence of abnormal hair on various parts of the body is charted in table 26 It is probable that the presence of hair about the areola is a more important sign than hair on the face, for hair on the lip is a very common occurrence among the darker skinned people, and hair on lip and chin may be merely evidence of senescence

The feature of possible importance in table 26 is the occurrence of a moderate amount of areolar hair in 28 and 50 per cent, respectively, of the women with fibro-adenomas and "painful nodules," and of marked breast or sternal hair in a smaller number Such abnormalities

TABLE 24—*Hair Color*

	Premenopause					Menopause					Postmenopause					Totals				
	Available Cases	Black	Brown	Blonde or Red	Gray or White	Available Cases	Black	Brown	Blonde or Red	Gray or White	Available Cases	Black	Brown	Blonde or Red	Gray or White	Available Cases	Black	Brown	Blonde or Red	Gray or White
Fibro-adenomas	17	6	6	4	1	1	0	1	0	0	1	0	0	0	1	19	6	7	4	2
Painful nodules	19	4	10	5	0	1	0	0	1	0	0					20	4	10	6	0
Chronic mastitis	25	17	3	4	1	17	8	1	2	6	2	1	0	0	1	44	26	4	6	8
Papillary tumors	3	1	2	0	0	3	2	0	0	1	1	0	0	0	1	7	3	2	0	2
Total benign	64	28	21	13	2	22	10	2	3	7	4	1	0	0	3	90	39	23	16	12
Malignant	31	17	8	5	1	51	22	5	6	18	40	8	0	0	32	122	47	13	11	51

were practically nonexistent among the older women with chronic mastitis or carcinoma and not at all frequent among even the younger patients with cancer

HEREDITY

Estimates of the frequency of previous cancer in the family of women suffering from carcinoma of the breast have, according to Lane-Claypon, varied from 13 to 37 per cent In her own most carefully checked series based on the cause of death of parents only, Lane-Claypon found the evidence for heredity rather slight, since the occurrence of cancer in one parent was 103 per cent for the cases of cancer and 81 per cent for the control women

That such attempts to find evidence of a hereditary factor in cancer will always be unsuccessful seems highly probable, for there is practically no clinical evidence nor biologic reason for thinking that a

TABLE 25—Racial Distribution

TABLE 25—Racial Distribution																								
	Premenopause					Menopause					Postmenopause					Totals								
	Available Cases	North European	Jewish	Latin	Colored	Others	Available Cases	North European	Jewish	Latin	Colored	Others	Available Cases	North European	Jewish	Latin	Colored	Others						
Fibroid adenomas	11	18	12	7	1	1	29	13	17	3	2	7	61	27	11	3	5	3	152					
Painful nodules	26	11	3	2	0	1	13	8	16	0	1	1	5	3	2	0	0	0	100					
Chronic mastitis	25	12	10	3	2	1	11	5	15	0	1	0	1	1	0	0	0	0	11					
Papillary tumors	6	1	2	0	0	1	11	3	0	0	0	0	3	1	0	0	0	0	15					
Total benign	73	12	16	8	3	1	33	17	3	2	7	19	27	11	3	5	3	0	62					
Malignant	11	8	12	7	1	1	29	13	17	3	2	7	61	27	11	3	5	3	82					

TABLE 26—Hypertichosis																								
	Premenopause					Race	Menopause																	
	Fibroid	Colored	Latin	Jewish	Others																			
1	1	1	1	1	1																			
2	1	1	1	1	1																			
3	1	1	1	1	1																			
4	1	1	1	1	1																			
5	1	1	1	1	1																			
6	1	1	1	1	1																			
7	1	1	1	1	1																			
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97	1	1	1	1	1																			
98	1	1	1	1	1																			
99	1	1	1	1	1																			
100	1	1	1	1	1																			

TABLE 26—Hypertichosis

TABLE 26— <i>Hypertichosis</i>																												
Premenopause					Menopause					Postmenopause					Totals													
Fico		Breast			Fico		Breast			Fico		Breast			Fico		Breast			Fico		Breast						
Available Cases	Per Cent Marked	Slight	Moderate	Marked	Available Cases	Per Cent Marked	Slight	Moderate	Marked	Available Cases	Per Cent Marked	Slight	Moderate	Marked	Available Cases	Per Cent Marked	Slight	Moderate	Marked	Available Cases	Per Cent Marked	Slight	Moderate	Marked	Per Cent Marked	Per Cent Marked	Per Cent Marked	
Uterine adenomas	18	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Painful nodules	18	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Chronic mastitis	25	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Papillary tumors	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Total benign	19	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Malignant	11	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	

tendency to the inheritance of cancer in general exists. It is, for example, impossible to believe that a history of squamous carcinoma of the tongue in the grandfather of a woman with cancer of the breast is of any importance. A history of carcinoma of the endometrium, of a fibro-adenoma of the breast or even of a myoma of the uterus is possibly of significance, while a previous case of cancer of the breast in the family is probably worthy of serious consideration.

Certain single striking instances of the multiple occurrence of specific forms of cancer in a family have from time to time been published, and among these, instances of the inheritance of breast cancer are frequent. There is, for example, the family tree published by Broca in which sixteen cases of cancer occurred in four generations among thirty-three persons and of these sixteen, eleven were localized in the breast, three in the liver (metastatic?), one in the uterus and one in the stomach. The case of gastric cancer was the only one of the group to occur in a male.

A still more extraordinary instance of apparent heredity is that reported by Leschcziner of a mother and three daughters who each developed breast lumps early in life at the respective ages of 21, 14, 24 and 19. Three eventually died and the fourth had recently been operated on at the time of the report. In each the diagnosis was carcinoma and in the three in which the sections could be studied the tissue showed adenocarcinoma with some colloid degeneration.

In a study of the family histories of the present group (table 27) it was found that 6 per cent of the women of the entire series (271 cases) knew of a previous case of cancer of the breast in their family. It is also to be noted that five of the patients reported two cases of previous mammary neoplasm in their family (table 27).

It was thought that perhaps next to actual cancer of the breast some significance might be attached to the previous occurrence of other forms of genital tumors, but the table fails to give evidence of this. The question of fibroid tumors and goiters in the family was not, however, carefully gone into with each patient.

One rather striking fact is that the family history of cancer is rather higher in percentage among the women with benign tumors of the breast than those with malignant. This relationship is further support of the contention that if a hereditary factor exists, it is in the nature of a predisposition to irregular proliferative processes in general and not to malignancy in particular.

An attempt to correlate the physiologic era of development of cancer in the patient with that in which she developed her tumor failed to lead to any results. The family of Leschcziner showed apparently an inheritance specifically dependent on certain constitutional





peculiarities of puberty. A similar relationship might conceivably exist between cancer and certain hereditary peculiarities of response to the menopause.

The hereditary factor in mammary tumors appears undoubtedly to be a predisposition only, suppressed or brought to the surface by the character of the physiologic processes that the patient's life has accidentally brought to her breast. It is difficult to imagine on what other basis such a predisposition can rest than on an hereditary anomaly of the constitution of the reproductive system.

#### THE HISTOLOGIC FORM OF CANCER OF THE BREAST IN RELATION TO ETIOLOGY

A part of the original plan of this study had been to separate the different microscopic forms of cancer of the breast from each other and to examine individually the etiology of various types. Unfortunately, it was found that in only a small proportion of the cases was there available pathologic material suitable for making the finer diagnosis of special types of cancer.

That such a study might shed a light on the cause of cancer of the breast is clear from the following considerations:

(A) *Form and Location*—The various sections of the breast, large ducts, small ducts and acini, are physiologically different in their reactions, variably responsive to endocrine stimulation and diversely subject to chances of inflammation. The striking contrast afforded in the uterus by the biology of cervical and fundal cancers is illustrative of the diversities that may exist between the strictly parenchymatous and the ductal portions of an organ. That Paget's disease of the nipple is an essentially different type of lesion from the adenocarcinoma of the finer ducts and acini is probable. Differences dependent on their points of origin may also exist between the etiology of many special forms. It is for these reasons that, although endocrine influences appear to be important factors in initiating atypical cell proliferation in the breast, the idea of other agencies being sometimes effective cannot be discarded.

(B) *Form and Physiologic Phase*—Beside the question of whether histologic form is related to the site of origin of the tumor, there is the problem of whether tumor architecture is connected with the physiologic phase in which the breast happens to exist at the time of the genesis of the new growth.

The few cases that could be assembled for this study afford a little evidence to show that certain tendencies do exist for different forms of cancer to develop under special circumstances (table 28).

(1) *Age*. Adenocarcinoma is the predominant tumor of early life but also occurs in the aged. Other forms are scattered but in general



That the opposite of this theory may also be true, namely, that the less differentiated forms of cancer of the breast are less related to the benign lesions and hence perhaps governed by different etiologic factors such as senile involution, trauma and infection, remains a possibility

### RÉSUMÉ

That the breast epithelium is normally responsive throughout life to stimulation by the internal secretion of the ovary has been shown at considerable length in the first sections of this paper. At the same time it must be clear that when the ovarian activity manifests itself in a regularly recurring cycle proliferative and regressive processes in the genital organs balance each other so nicely that during normal adult life no actual growth takes place.

From the point of view of clinical observation, the condition necessary for breast growth is the presence of a partially active ovary which is not producing a menstrual cycle. Such is the normal state before puberty and during pregnancy. A similar intermediary stage of ovarian activity must exist for a longer or shorter time at the menopause as the sex glands pass from the state of full activity to complete extinction.

Beside these relatively normal occasions in which breast proliferation may occur, there are certain abnormal endocrine states in younger women which may closely simulate one of those just noted and in which conditions also appear to be correct for breast growth. The first of these is seen in women whose reproductive system never completely developed and whose organs and body form resemble those of a girl at puberty. The second is that of acquired hypofunction of the ovary, manifesting itself in increase of weight, menstrual disorders and other symptoms usually associated with the menopause.

It has been my purpose in this paper to assemble the evidence in favor of the theory that tumors of the breast of practically all varieties are not only logically but also actually dependent on abnormal variants of the physiologic endocrine states that normally produce breast growth.

Clinical observations indicate that special forms of tumor of the breast tend to be associated with particular types of the disorders that have been described.

*A* The fibro-adenoma occurs typically in breasts that are a part of a generally underdeveloped reproductive system and under conditions in the body somewhat similar to those existent at the time of the development of the breast at puberty. This view is consistent with the highly organic character of the histology of this tumor and the fact that it is frequently a rather faithful reproduction of the normal gland. It is also not incompatible with the theoretical view that the fibro-adenomas are derived from previously undeveloped "fetal" rests.

The reasons for believing that the women of the fibro-adenoma group are backward in development and are suffering from a special form of glandular derangement are the following

- 1 The great majority are unmarried
- 2 Few have had children
- 3 Among those who have borne children, few have nursed them successfully
- 4 There is a high incidence of irregular menses, especially of the shortened interval type, and the duration of the periods tends to be long These irregularities date from puberty and are not acquired
- 5 Dysmenorrhea is common, and being present is indicative of hypoplasia uteri
- 6 Premenstrual breast pain is marked and, as a rule, has been present since puberty
- 7 The incidence of acquired pelvic disease is low
- 8 The thyroid is often slightly enlarged, a condition frequently met with in adolescence The conception of Biedl that there is thyroid dominance during childhood until its activity is suppressed by the maturing sex glands may be cited to indicate further that the women of this fibro-adenoma group are still for all practical purposes in an adolescent stage
- 9 The breasts are small and erect with small nipples and areolae and often with a little excessive hair
- 10 The patients themselves tend to be slender and a little underweight, possibly further proof of their "adolescent" state

*B* Chronic mastitis occurs as a secondary proliferative process in breasts that have at one time attained a considerable degree of development but which have passed through an involutional period It arises under conditions of irregular, but apparently, as a rule, declining ovarian activity Such conditions exist typically during the years preceding the cessation of menstruation at the climax but also in younger women with a disturbance of the ovarian function These views are consistent with McFarland's theory that the cysts are evidence of an incomplete involution after a lactation hypertrophy and with Cheate's teaching that the essential feature of the disease is a hyperplasia It is of course, clear that "chronic mastitis" is a misnomer, some such term as "fibro-adenosis" being preferable in my opinion (Note Semb's use of word "fibro-adenomatosis")

The reasons for believing that chronic mastitis is a secondary proliferative process occurring in involuting breasts under the influence of irregular ovarian function are the following

- 1 The greater number of the women with this disease are married
- 2 The majority have had children
- 3 The fact that the percentage of nursing failures was relatively low indicates that the breasts were once normal

4 A considerable number of cases occur just before the menopause or in actual association with the menstrual irregularities preceding cessation. The frequency of menstrual abnormalities in the younger women indicates that a subnormal ovarian function exists in these cases which is potentially similar to that of the menopause.

5 Dysmenorrhea is rare.

6 Premenstrual breast pain is unusual in the older women with chronic mastitis, but is fairly frequent in the younger women.

7 The incidence of acquired pelvic disease is fairly high.

8 Thyroid hypertrophy is unusual.

9 The breasts are as a rule pendulous with large nipples and wide but often colorless areolae.

10 The body weight tends to run a little above the normal for the age, and recent increases in weight are common.

C The "painful nodules" are at best an ill defined and somewhat arbitrarily collected group. The more localized examples are difficult to separate from the fibro-adenomas, and the more diffuse from the cases of chronic mastitis. It should be noted in particular that in the early age group many of the cases of chronic mastitis, so classified on account of the palpably diffuse nature of the process, should perhaps etiologically have been placed with the cases of painful lump.

In general, it may be said that the examples of this entity often give the impression of being partly dependent on a slight developmental deviation from the normal, but the essential feature is the presence of a new proliferative stimulus being applied to a breast which is still in the period of full maturity and in which involutional changes are decidedly not prominent.

The reasons for taking this point of view are the following:

1 The majority of the women are young.

2 Only about half of the women have had children.

3 Success in nursing has not been as universal as in the cases of the women with chronic mastitis.

4 Abnormal menstruation, often of an acquired type, is more common than with any other form of breast neoplasm in young women.

5 Dysmenorrhea is fairly frequent but not so prominent as in the case of the patients with fibro-adenoma.

6 The premenstrual breast signs are extremely marked, a fact indicative of excessive corpus luteum stimulation.

7 The incidence of acquired pelvic disease, especially of an inflammatory character, is high.

8 The thyroid is almost constantly slightly full.

9 The form of the breast offers nothing characteristic.

10 The general body form and weight tend toward slenderness.

The conditions favorable to the formation of these growths have been discussed as if only three distinct types existed. Such is obviously not the case, for it has already been pointed out that morphologic varieties of tumor tend to be connected by transitional forms and the much less tangible conditions of etiology are, as might have been expected, still less sharply defined. Furthermore, since the characteristics of etiology of tumor forms as outlined are based entirely on percentages which never approach the hundred mark, it must be evident that they are representative of tendencies only.

*D* The relation of the ovarian function to the formation of malignant tumors of the breast is much less clear than it is for the benign forms, yet two facts derived from the histologic studies of the pathology of the breast indicate that for some cancers at least all that has been said about the benign tumors may be said about the malignant tumors also. The first of these points is the debated theory of the origin of malignant tumors from the benign ones, and the second is the absence of any sharp histologic line between differentiated adenocarcinomas and relatively actively growing benign tumors.

In order to relate the development of cancer to abnormalities of the ovary, certain suppositions are necessary.

- 1 In women in whom malignant growths develop before the menopause, cancer may arise under various conditions of abnormal ovarian activity. A single type of abnormality will not explain it. Thus it must be assumed that in different women cancer may appear under the conditions noted for the fibro-adenomas, for the "painful nodules" or for chronic mastitis. In other words, it may be related to the disturbances of ovarian activity incidental to puberty or to an ovarian anomaly describable as a delayed puberty, to an unknown disturbance during pregnancy, to the irregularities of the menopause or to a hypo-ovarianism in younger women that simulates the menopause state. Granted this supposition that cancer may be related to any of these phases of disturbed ovarian activity, practically every case among the younger women in the present group could be explained.

- 2 The late carcinomas of the breast can be related only to the ovarian function by assuming that they are derived from benign or malignant cell rests quiescent since the time preceding the extinction of the ovarian influence. Such a theory is not to be lightly rejected since if carcinoma is derived from benign hyperplastic epithelial tissue, its ultimate origin must date back to the menopause, for it appears that benign processes rarely, if ever, have their inception after the ovary has completely ceased to be active.

Another reservation is also to be made for it must be clear that the indicated conclusions of the present study pertain only to the origin of tumors in general and not at all to the cause of malignancy in particular since practically all the anomalies of the sexual function that were noted were found equally frequently in the benign and malignant series. The point reached therefore is that at which most clinical studies on the genesis of cancer actually though not always admittedly,

terminate It is the point where one must somewhat lamely postulate that the cause of cancer is the same as that of the precancerous lesion with the possible addition of the accumulative effects from a longer or stronger stimulation by the original agent or the hypothetic cooperation of an individual or age predisposition of the tissues

In spite of many reservations there is considerable evidence that ovarian dysfunctions are concerned in the production of cancers of the breast

1 The fact that most reports indicate a greater predisposition among unmarried women indicates that the cases, if any, due to inflammatory conditions of the puerperium are rare since they must weigh so little in the gross statistics

2 The lower fertility among women with cancer, as reported by several writers, is suggestive of relatively frequent pelvic disease

3 Failure to nurse in a normal manner, a factor often stressed by students of the etiology of cancer of the breast, appears from an investigation of the causes of these failures to be due almost entirely to insufficient secretion, an internal factor connected with the constitution of the reproductive system

4 A large percentage of the cases of cancer of the breast occur just before, during or immediately after the menopause when abnormal stimulation of the breast by the ovary may be assumed Among the younger women with cancer of the breast many have suffered from a recent change in the type of their menstrual periods, an indication of changing conditions in the ovary Among the older women, the growths may represent the gradual malignant transformation of abnormal epithelial tissues that took origin at the time of the menopause

5 Dysmenorrhea is of moderate frequency among the younger women with cancer of the breast, indicating that certain of these early cases may have been produced under conditions similar to those under which fibro-adenomas arise

6 Premenstrual breast pain is frequently a symptom noted as having appeared for the first time shortly before the discovery of the tumor and is evidence of a recently acquired, excessive corpus luteum effect on the breast

7 The history of an acquired pelvic disease or of a major gynecologic operation is met with extraordinarily often in the study of patients with breast cancer and suggests the possibility that abnormal proliferation in the breast may at times depend on an ovarian function disturbed by the results of pelvic inflammations or congestions

8 The thyroid often shows some abnormality, such as diffuse enlargement in the younger or nodular goiter in the older patients The significance of this change rests on the probable existence of a common stimulus producing the two tumor forms, since under physiologic conditions both organs usually hypertrophy simultaneously

9 Cancer occurs in all types of breasts, but in the younger women it is more common in the small erect breast, similar to that which appears to be especially susceptible to the fibro-adenoma, while in the older women it occurs chiefly in breasts which are also the seat of chronic mastitis

10 The body weight in cases of breast cancer was below the average for normal women in the early age groups and above the average in the later period In this respect the women with cancer followed the tendency noted on the one hand for the fibro-adenomas, and on the other for the cases of chronic mastitis

To be in harmony with the theory that an internal, endocrine disturbance is the cause of tumors of the breast, the factor of heredity must be effective through the medium of a special type of inherited genital constitution which is so predisposed as to produce atypical breast proliferation in certain of the physiologic eras of life. If such is the case, no tumors are significant in the family history except those of the breast and perhaps of the other organs connected with reproduction. On the other hand, it appears that the hereditary factor is not always specific as to the exact form which the tumor of the breast may assume, but manifests itself as carcinoma in one generation and as a benign tumor in another.

### CONCLUSION

The parenchyma of the breast has been shown to depend on the sexual cycle for all its normal variations of structure and to be capable of rapid growth and transformations under certain physiologic conditions of ovarian activity. In this respect the breast is similar to the endometrium, the thyroid and certain ovarian structures. Pathologically, the various forms of tumor of the breast have their counterparts in the tumors of the three organs mentioned and of the prostate. What clinical observations can be collected from the literature and from this study of 271 cases indicate that etiologically the tumors of the breast, including carcinoma, are closely related to those of the endometrium, thyroid and ovary, are somewhat allied to myomas of the uterus and are in a way equivalent to tumors of the prostate. The tumors of these five organs, therefore, form a group, the etiology of whose members shows many points of mutual resemblance. To attempt to relate inflammatory accidents of lactation to cancer of the breast is to classify it etiologically with cancer of the cervix, which on both inductive and deductive grounds appears unjustifiable.

It is possible that the contrast afforded by the causes of origin of these two common types of new growth may lead to the formulation of a general principle. Such a principle would amend the teaching that cancer results from chronic irritation by adding that the stimulus must as a rule be of the same type as that to which the particular tissue is biologically best adapted to respond with proliferation. Such a conception would appear, superficially at least, to reconcile the conflicting theories of numerous authors, who have formed their opinions of the causes of cancer from the study of the new growths of entirely different tissues. With this view it would be entirely consistent for mechanical or chemical irritants to produce cancerous changes in the protective epithelial cells covering the surface of the body and lining the walls of the intestinal tract, for an infectious agent to induce new growth in lymphoid, myeloid or granulomatous tissue for trauma to produce tumors by evoking the reparative function of fascial and osteogenic cells



and finally for hormonal influences to be effective in producing hypertrophy, hyperplasia and neoplasms in the breast and other organs whose normal growth processes are under endocrine control

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# INDUCED PARALYSIS OF THE DIAPHRAGM\*

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Induced paralysis of the diaphragm imitates spontaneous paralysis which is a natural protective reaction to divers pleuropulmonary irritations. The capacity of the thoracic cavity of the side affected, or of both sides if the paralysis is bilateral, is reduced by the upward displacement of the diaphragm.

A further reduction frequently results from a correlated increased declivity of the ribs and narrowed intercostal spaces (figs 1 and 2). Moreover, the excursions of the ribs are restricted. Induced and spontaneous paralysis may be incomplete or complete, unilateral or bilateral, transient, temporary or permanent.<sup>1</sup>

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Submitted for publication, Feb 27, 1930

\* The experimental observations on which the clinical work was based were conducted in the Ambulance de L'Océan at LaPanne (1917), the Central Laboratories of the A E F (1918), and at Columbia Hospital (1919-1920) under grants from the American Red Cross. The clinical work was done in various hospitals for nontransportable wounded of the First Army, A E F, in the Murdale Sanatorium for Tuberculosis of Milwaukee County, in Mount Sinai and Columbia Hospitals, Milwaukee.

Evidence for statements made in this communication can be found in the following: Yates, *Wounds of the Thorax*, in *Oxford Surgery*, London, Oxford University Press, *Wounds of the Chest*, in the Medical Department of the U S Army in the World War, 1927, vol 11, pt 1, pp 343-442, *Effects of Acute and Chronic Pneumothorax*, *Am J M Sc* **165** 1, 1923, *The Significance of Vital Capacity in Intrathoracic Therapy*, *Arch Surg* **10** 477 (Jan) 1925, *The Significance of Vital Capacity in Intrathoracic Therapy*, *ibid* **12** 257 (Jan) 1926, *Rationale of Operations Helpful in Promoting Recoveries from Pulmonary Tuberculosis*, *ibid* **14** 369 (Jan) 1927, *Pulmonary Tuberculosis*, *ibid* **19** 1122 (Jan) 1929. Yates and Raine, *Diseases of the Lymphatics*, in *Practice of Surgery*, Hagerstown, Md, W F Prior Company, 1929, vol 3, chapter 9.

1 Upward displacement is caused by the action of negative intrapleural pressures and positive intra-abdominal pressures on a more or less inert diaphragm unless pleuritic adhesions at the base are strong enough to prevent it. Increased declivity of the ribs and narrowing of the intercostal spaces is more constant and greater if the muscle is atonic as well as paralyzed. This effect on the levator costal and intercostal muscles is apparently produced by some reflex inhibition probably through the sympathetic nerves. Paralysis and consequent elevation of the diaphragm affect animals with thin pleurae and those with thick pleurae similarly. Human beings have thick pleurae. The mediastina of animals with thin pleurae are neither air-tight nor water-tight. The mediastina of those with

Occasionally a transient bilateral paralysis is induced to arrest singultus, or a transient unilateral paralysis is used to facilitate trans-abdominal repair of diaphragmatic hernia. Commonly, temporary and permanent paralysis and atonicity are induced for purposes to be discussed later because of the following responses

Reduction in the capacity of the thoracic cavity imposes a corresponding diminution in the volume of the lung. Restricted movements of the parietes limit the excursions of the lung to those slightly above and below the level of mean inflation

Reduction of the volume of the lung approaches but does not reach the position of collapse (which occurs if negative pressures are abolished) when complete paralysis and atonicity are induced and the ascent of the diaphragm is not impeded by adhesions. Under these conditions the lungs and visceral pleura of human beings and animals with thick pleurae receive the largest unit volumes of blood through the bronchial vessels, and the lungs receive the largest volumes of blood through the pulmonary vessels<sup>2</sup>. Both blood volumes are delivered with less than usual cardiac labor because peripheral intravascular resistance is so nearly minimal. Material restriction of pulmonary excursions curtails the dissemination of noxious substances from pleuropulmonary lesions and does not interfere with healing which can be almost scarless

Thus induced paralysis which, be it reemphasized, is an imitation or rather a reproduction of natural protective reaction to some pleuropulmonary irritations, accomplishes two extremely beneficent results. It shields the subjects from intolerably rapid dissemination of toxic products, bacteria and tumor cells from inflammatory and neoplastic lesions. The maximum units of blood delivered assure that the lungs and visceral pleura will realize the utmost of their power of resistance, defense and repair<sup>3</sup>

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thick pleurae are both air-tight and water-tight. Elevation of one side of the diaphragm in the former reduces intrapleural negative pressures equally in both sides of the thorax, in the latter, only in the side affected. Moreover, the compensatory emphysema which occurs automatically with unilateral diaphragmatic paralysis in the contralateral lung prevents displacement of the mediastinum toward the unaffected side if the circulatory apparatus is competent, it may even cause displacement toward the affected side

2 Andrus and Wilson (*Arch Surg* **19** 1205 [Jan] 1929) showed that this effect is produced in both lungs of animals with thin pleurae (dogs) if one side of the diaphragm is paralyzed

3 Resistance, defense and repair are produced by the activities of tissue cells, supported, stimulated and supplemented by the cellular and noncellular constituents of the blood delivered to them. If they are adequate, they confer insusceptibility. If slightly less adequate, disease is inaugurated but recovery occurs. If they are more inadequate death is inevitable. Therapy is successful as it increases the quantity of blood delivered to lesions and improves the quality of blood in circulation, and, when necessary, restores its volume



These benefits are purchased at a price. Paralysis of one side of the diaphragm reduces vital capacity upward of 10 per cent even when the lungs are little affected and the myocardium is competent. Vital capacity measures the efficacy of external respiration which determines the capacity of a person to work and to survive. Paralysis of both sides of the diaphragm more than doubles the handicaps of unilateral paralysis.



Fig 1—J W, Muirdale Sanitarium, March 25, 1924, aged 28. Roentgenogram taken at the end of inspiration. There is limited spontaneous paresis of the right side of the diaphragm, and coincidental narrowing of the intercostal spaces on the right side. Phrenemphraxis performed on April 8, 1926, induced complete paralysis but not atonicity. Severe crushing was employed to protract effect.

The technical problems involved in the induction of paralysis are now obvious, namely, how to induce complete paralysis and atonicity simply and dependably and how to induce transient, temporary and permanent paralysis so that the handicaps imposed need not exceed benefits conferred.

Motor impulses are transmitted to the diaphragm in human beings with rare, if any, exceptions, through the phrenic nerves and their aberrant or accessory branches. Some of the impulses that maintain the tonicity of the diaphragmatic muscles are transmitted through fibers in the sympathetic nerves. Numerous anatomic studies have revealed that aberrant and accessory branches arise from phrenic nerves and from

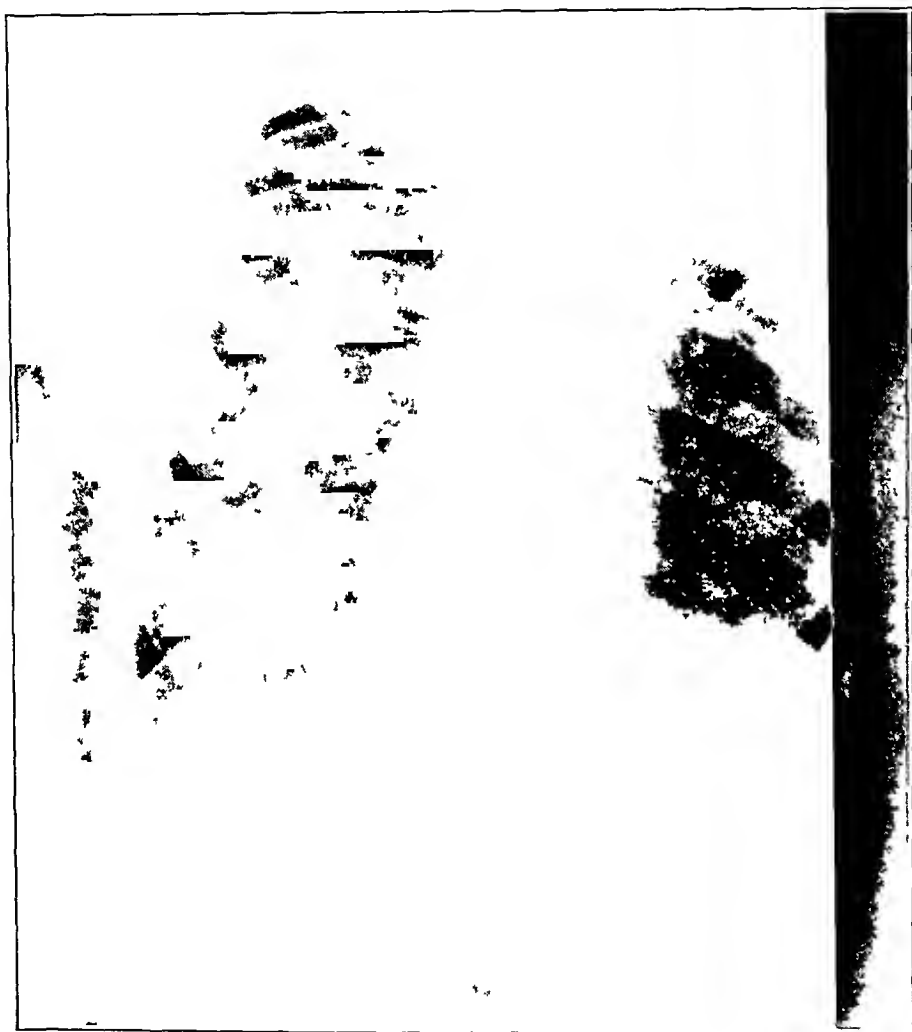


Fig 2—J W, Muirdale Sanitarium, Dec 20, 1929, aged 34. Roentgenogram taken at the end of inspiration. There is incomplete recovery of motion of the right side of the diaphragm. Increased declivity of the ribs and narrowing of the intercostal spaces (right) has reduced capacity of the right side of the chest materially and has induced obvious compensatory emphysema in the left lung. The mediastinum was thereby displaced slightly to the right.

then constituent third, fourth and fifth cervical roots in more than one half of all people and that these branches may take divers pathways to reach the diaphragm. Some run independently and are aberrant, others

fuse with the nerve to the subclavius muscle, a few fuse with the descending branch to the omohyoid, and are to that extent accessory. Aberrant and accessory branches arise because of failure to fuse or to remain fused with other phrenic fibers. Aberrant twigs usually lie quite parallel to the main phrenic trunk, some barely separated from it, others are more remote, and may lie anterior, lateral or medial to the trunk. They may continue as separate nerves to the diaphragm or may fuse with the main trunk at different levels, thus forming loops which some times include other structures, e. g., the thoracic duct of subclavian vein. Accessory branches join the nerve to the subclavius muscle or the ansa hypoglossi, then leave them to continue downward either as separate branches to the diaphragm or to fuse with the main phrenic trunk within the chest. Fibers of sympathetic nerves that transmit tonic impulses to the muscles of the diaphragm may join the phrenic nerves in their upper or lower cervical or intrathoracic portions or may reach the diaphragm independently.

Experimental studies and about 300 operations performed on human beings have led to a development of methods that satisfy the following requirements

An incision that will offer a direct approach to the lower anterior surface of the scalenus anticus muscle on or near which the main trunk of the phrenic nerve will be found

Subcutaneous dissection that will provide adequate exposure safely and simply and permit of closure that leads uniformly to good healing without interference with function and with an insignificant scar

Means to determine during operation when all the fibers that transmit motor impulses have been blocked and complete paralysis has been induced because, as already stated, aberrant and accessory branches are more often present than absent, but infrequently contain motor fibers. Consequently, the wider dissections needed to discover and to block them are usually futile and are more or less harmful as the branches transmit useful impulses

Means to determine during operation when the fibers that transmit tonic impulses have been so effectively blocked that the upward displacement of the diaphragm may suffice to provide the most beneficial diminution in lung volume and restriction of its excursions

Measures by which the transmission of all motor impulses may be interrupted for a few days, weeks or months or permanently

#### OPERATIVE TECHNIC

The operation is performed with the patient under local anesthesia (1 per cent procaine hydrochloride), and lying on a fluoroscope table. Ten grains (0.65 Gm.) of sodium barbital given an hour before operation to eliminate the slight risk of poisoning from the anesthesia and to limit apprehension. If the left phrenic nerve

is to be blocked and exeresis is a possibility, the patients are given a glass of cream a half hour previously so that if the thoracic duct is torn the discharge of chyle is immediately obvious, and ligation of the duct is facilitated

If the left nerve is to be blocked and the lower left side of the chest is so dense that the diaphragm cannot be recognized fluoroscopically, patients are given carbonated water to create a contrast gas bubble in the cardia of the stomach

A transverse incision is made in a skin crease just above the clavicle. It extends from 1 inch lateral to the outer margin of the sternomastoid muscle inward 1 or 2 inches mesial to that margin and exposes the anterior surface of the muscle. The superior lip is freed and retracted upward, fibers of the muscle are separated and retracted laterally, exposing the deep fascia (fig 3)

Palpation locates the scalenus anticus muscle, and this determines the approach. In some persons the internal jugular vein overlies the muscle, in others, the

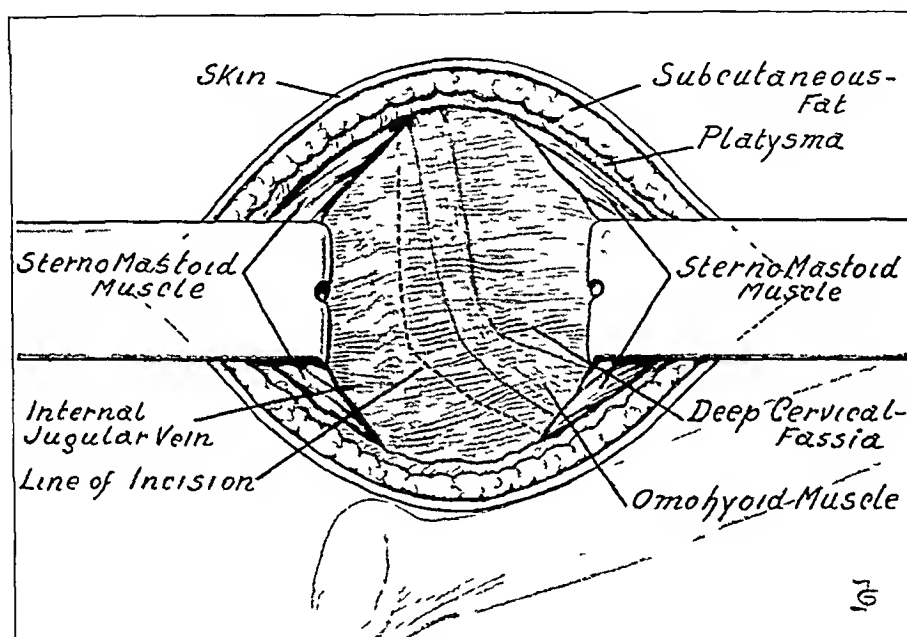


Fig 3—Dissection carried down to first layer of deep cervical fascia, sternomastoid split and retracted mesially and laterally

muscle is lateral to the vein. If the vein overlies the muscle, its lateral border is exposed<sup>4</sup> and the vein is retracted mesially (fig 4), otherwise it is not disturbed. The deep fascia is divided close to the mesio-inferior border of the omohyoid. The muscle is retracted laterally and the fascia mesially (fig 3) exposing the layer of fat in front of the scalenus anticus muscle. Within this fat lies the transverse cervical artery and lymph glands, which may be considerably enlarged in patients suffering from pulmonary tuberculosis affecting the upper lobes. Blunt dissection usually quite painless, makes it possible to expose the prevertebral fascia overlying the scalenus anticus muscle to which the phrenic nerve is usually attached without injuring the transverse cervical artery. It is

<sup>4</sup> Care must be taken to see the lateral wall of the vein which may be collapsed before incising adjacent structures. Serious even fatal hemorrhages, and air embolism have been caused by failure to take this precaution.

desirable not to infiltrate the fat with procaine hydrochloride, as this may desensitize aberrant fibers. Rarely the lymphomas are so large and numerous that some of them must be excised to obtain exposure of the prevertebral fascia.

Lateral retraction of the margins of the aperture in the layer of deep fat permits identification of the main trunk of the phrenic which is freed by incising the fascia along its margins. A loop of thread is passed around the nerve and used as an elevator. If a transient paralysis is indicated, a few drops of 1 per cent cocaine are injected intraneurally. Fluoroscopic examination reveals whether or not the diaphragm is adequately paralyzed. If not, aberrant or accessory branches containing motor fibers are found and infiltrated or slightly crushed. Usually temporary or permanent paralysis is desired. The nerve is held loosely between the blades of a sharp hemostatic forceps, the lights are extinguished, the x-rays generated and the diaphragm visualized. Closing the clamp abruptly causes

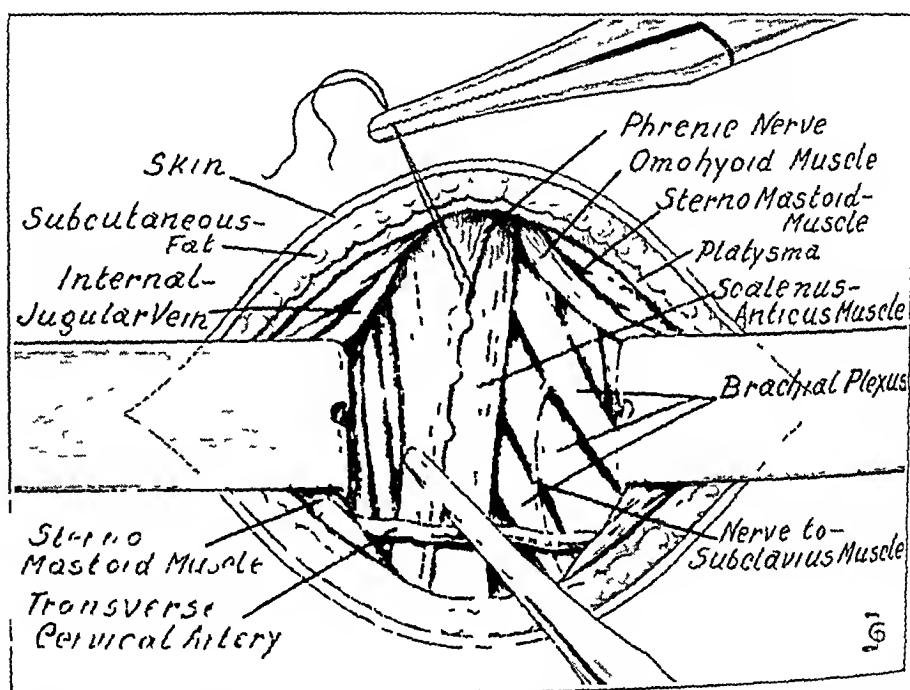


Fig 4—Dissection completed and nerve crushed. The incision and retraction shown is greater than that employed but is shown here to give the anatomic relations of adjacent structures.

an immediate contraction of the muscle, followed by relaxation and displacement upward. If all motor fibers have been blocked, the contour of the diaphragm is rounded and immobile save for the traction exerted by the other half of the diaphragm at the end of deep inspiration. If not, wavy undulations appear during inspiration produced by contraction of the unparalyzed fibers. Then it is necessary to locate aberrant and accessory branches and to repeat the crushing until the paralysis, as shown by the fluoroscope, is complete. Motor fibers are more commonly transmitted through aberrant than accessory branches, and if present in the accessory branches are more often in the nerve to the subclavius muscle than in the nerve to the omohyoid. The reason for not infiltrating the deep fat with procaine hydrochloride now becomes apparent.

The main trunk of the phrenic nerve contains both motor and sensory fibers and when irritated it produces pain referred to the back of the shoulder or neck.

It sometimes lies in anomalous positions and can be identified by the pain caused if it is pinched. So too the aberrant and accessory branches may contain both motor and sensory fibers though they may contain neither. Aberrant twigs are often so small that identification is difficult but the pain produced by pinching frequently is helpful in identifying them. Similarly the provocation of pain makes the identification of the nerve to the subclavius easier. Occasionally it is necessary to crush all of the deep fat adjacent to the aperture to induce complete paralysis.

When the transmission of the tone impulses is blocked effectively, the diaphragm is not only displaced to a higher level which would not of itself be recognizable, but it is also rendered so atonic that a paradox appears. The paralyzed side rises during inspiration. A paradox appears immediately or after a few days in a majority of those in whom the induced paralysis is complete. It is as yet uncertain whether there is any material difference in the benefits conferred between complete paralysis with and without effective atony.<sup>5</sup>

Once the nerve or nerves that contain fibers which transmit all motor impulses to the diaphragm have been identified it is possible to induce temporary paralysis of approximately desired duration (phrenemphraxis). Crushing nerves moderately severely in two places will be effective for eight or ten weeks; crushing them severely in four places will protract paralysis for three or four months. More severe crushing in five places will induce paralysis of longer duration but recovery is uncertain either the nerve fibers do not regenerate or the degeneration in the muscle cells is irrecoverable. It now seems likely that when preliminary crushing induces a paradox, the total crushing should be less severe to avoid the degeneration that imposes permanent paralysis.

Permanent paralysis is induced either by resection of an inch or more (phreniectomy) of nerves containing motor fibers or by the division of such nerves and extraction of their distal portions (exeresis). Phreniectomy is preferable when the paralysis induced by crushing is complete and the atony is judged to be adequate. Pain is limited to the first crushing and there is no danger. When the paralysis caused by crushing is incomplete or the atony is inadequate the main trunk of the phrenic is divided and the distal portion gradually withdrawn. Extraction is painful if there are dense pleuritic adhesions; it is not always efficacious, and is not without danger. Intrathoracic hemorrhages have been reported. It is stated that a subclavian vein was torn, and a fatal hemorrhage resulted. We have noted tearing of the thoracic duct during the extraction of two left phrenic nerves. Both were ligated without producing symptoms. In one patient exeresis failed to induce complete paralysis. An aberrant or accessory branch which escaped detection extended independently to the diaphragm, or some motor impulses were delivered through fibers in the twelfth thoracic nerve. Moreover, exeresis

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5 The degree of pulmonary deflation approaches more closely the status of collapse if atony is effective and intravascular peripheral resistance is reduced to the limit of possibility, and probably the excursions of the ribs are minimized so that dissemination is restricted to the utmost unless the lung is immobilized. Complete immobilization of the lung automatically reduces unwholesomely the amount of blood delivered through the bronchial arteries which, unlike the pulmonary vessels, are under vasomotor control. It also introduces the atrophy of nonuse and curtails the activities of tissue cells. Bronchial arterial blood furnishes the lungs and visceral pleura in human beings with the bulk of nutrition and of the cellular and noncellular elements which contribute the major portion of resistance, defense and repair.

will not induce effective atonicity manifest in paradoxical inspiration when the fibers of the sympathetic nerves that transmit tonic impulses reach the diaphragm independently or unite with the phrenic below the level at which it tears

*Closure*—The margins of the aperture made in the deep fat by blunt dissection are approximated with a pursestring suture of fine catgut. The deep fascia and the fibers of the sternomastoid muscle are united with interrupted stitches. The subcutaneous fat and the platysma muscle are united with interrupted catgut stitches so placed that when tied the knots are buried deeply after the margins of cleavage in the sternomastoid have been sutured loosely. The skin is closed accurately with fine silk stitches (fig 5). When the hemostasis has been complete, if the skin stitches are removed on the second day and approximation maintained with strips of adhesive plaster, the healing is excellent and keloids exceptional.

*Postoperative Care*—Robust patients should remain in bed for three days to avoid tachycardia while the intrapulmonary circulation is becoming readjusted.

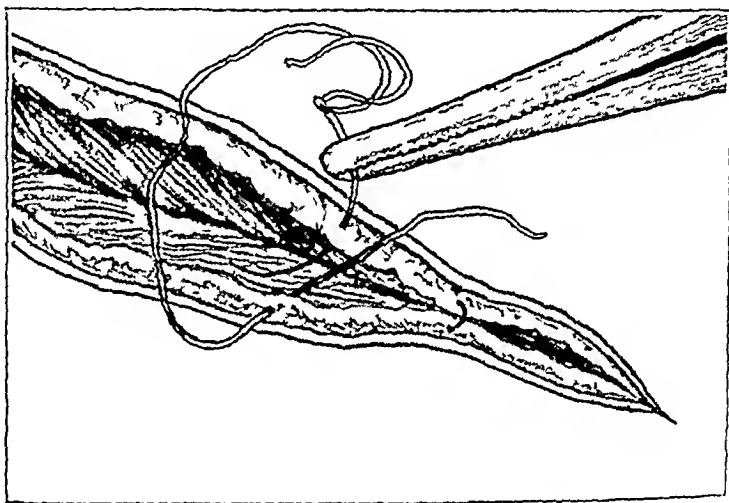


Fig 5—Closure of subcutaneous fat and platysma

III patients with advanced pulmonary lesions often suffer from tachycardia, increased cough and expectoration during this interval and need absolute rest

#### THERAPEUTIC ASPECTS

Clinical and experimental evidence suffices to explain and to prove the utility of induced paralysis, to define the states that make it futile, to indicate certain conditions in which it has not been but should be employed, and to disclose its disadvantages.<sup>6</sup>

6 Reduction in lung volume (partial deflation) and limitation of excursion not only increase pleuropulmonary powers of resistance, defense and repair, and restrict dissemination from lesions, but also the reduction in intrapleural negative pressures permits the walls of cavities in the parenchyma to collapse and facilitate the contractions of the wall of dilated bronchi. Alterations in intrapulmonary circulation which are favorable to patients who retain hematopoietic capacity and myocardial competence are futile in other patients whose blood-forming power are irreparably impaired, whose heart muscle is exhausted or whose lesions are

*Utility*—The sooner paralysis is induced, the larger the element of prophylaxis and the greater the benefits. A summary of personal observations and experiences follows.

*Empyema*—Acute. Induced paralysis is applicable only to interlobar and supradiaphragmatic forms, as spontaneous paralysis occurs when the diaphragm is involved. Temporary unilateral paralysis is then beneficial whether open or closed drainage is employed.

*Chronic*. This type occurs in two forms, tuberculous and nontuberculous. Permanent unilateral paralysis is beneficial when the diaphragm is not already immobilized reflexly or by dense adhesions. It limits the extent of subsequent thoracoplasty, if that is needed to promote healing.

*Abscess of the Lung*—Acute and Single. Temporary unilateral paralysis is beneficial when the abscess does not communicate with bronchi and postural drainage is impossible. It may obviate the necessity for external drainage.

*Chronic, Single or Multiple, Actinomycosis and Tuberculosis*. Permanent unilateral paralysis is beneficial if patients have not lost their capacity to make blood or the myocardium is not too weakened. It prolongs life and reduces the extent of subsequent thoracoplasty needed to promote healing.

*Pleuropulmonary Abscess*—Gangrenous. Permanent unilateral paralysis, if the abscess is large, or temporary paralysis if it is limited, hastens reduction of the cavity and lessens or eliminates subsequent thoracoplasty.

*Bronchiectasis*—Incipient. Temporary unilateral paralysis together with other measures, including postural drainage, may introduce recovery.

*Moderately Advanced*. Permanent unilateral paralysis may, if other measures are employed, lead to sufficient improvement to be satisfactory. If not, wide, extrapleural resection of the lower ribs will introduce recovery.

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prohibitively advanced. Incipient or impending, e. g., traumatic and operative, pleuropulmonary inflammations unaccompanied by paresis of the diaphragm occurring in less robust persons, particularly if there is myocardial weakness, can be made least ominous, distressing and probably shortened if a transient or brief temporary paralysis is induced. Reduction of 10 per cent in vital capacity in a robust person in whom induced unilateral paralysis is seldom indicated would be revealed by unusual dyspnea and tachycardia only in extraordinary physical exertion. Reduction of vital capacity would exceed 10 per cent after induced unilateral paralysis in a person having pleuropulmonary lesions and usually a weakened myocardium. Indeed, the limitation in external respiration might be prohibitive of even restricted physical effort. Bilateral induced paralysis produces even in the robust a transient dyspnea that simulates the consequences of breathlessness resulting from thoracic injury.



Advanced Permanent unilateral paralysis, wide resection of the lower six ribs and intercostal muscles and employment of other measures may produce satisfactory recovery. If not, the patients are prepared for the extrapleural lobectomy of Whittemore or the cautery lobectomy of Graham.

*Pulmonary Tuberculosis*—Incipient. Whether the disease is of the adult or infantile forms, temporary induced unilateral paralysis employed in conjunction with other measures, including proper exposures to sunshine and, when indicated, supplemented with transfusions of unmodified blood, promotes the most certain and rapid convalescence. Our experience indicates that this procedure if employed immediately after diagnosis is made, will materially reduce the duration and extent of disability.

Moderately Advanced. All measures are futile if the patients are highly susceptible, i. e. have lost hematopoietic capacity, which can be determined by blood counts and estimations of sedimentation rates repeated during an interval of several weeks while they are being given appropriate treatment, including transfusions of blood. Other patients who retain or can regain their blood-forming powers are benefited greatly by unilateral temporary or permanent paralysis. The healing of their lesions may suffice to obviate the need of thoracoplasty, or, if not to restrict the number of ribs that must be resected to permit of such healing. Sometimes a temporary paralysis must be made permanent if after the diaphragm regains activity the signs and symptoms indicate reawakening of the disease.

Advanced. A larger proportion of patients in this group have lost blood-forming capacity than in the preceding. Others have irreparable myocardial incompetence, still others have irreparably advanced lesions often bilateral. The balance can be benefited by permanent unilateral paralysis followed by more or less extensive thoracoplasty, particularly if bolstered by multiple transfusions. Some can be enabled to enter gainful occupations. In a few, it is said a temporary paralysis of the opposite side of the diaphragm may be helpful.

*Hemoptysis*—Hemorrhages (bright blood) from bronchial arteries are little affected by paralysis of the diaphragm. Hemorrhages from the pulmonary artery, in which the pressure is about one sixth of the systemic arteries, are usually promptly, and as a rule permanently controlled.

*Preparation for Thoracotomy*—Emergency. Emergency thoracotomies are performed to relieve injuries associated with hemothorax or hemopneumothorax and to relieve strangulated diaphragmatic hernia often resulting from trauma.

Hemothorax produces paresis of the diaphragm within an hour or two, later it becomes a paralysis. If when the chest is opened at the site of election (fifth rib) the diaphragm begins to contract, a transient paralysis (four days) should be induced by injecting 1 per cent cocaine into the phrenic nerve, which is easily reached in the position that lies on the pericardium. Should the chest be opened at a lower level, particularly when there is no hemothorax, it is safest to induce temporary paralysis by a cervical phrenic block half an hour or more before thoracotomy.

Thoracotomies, performed to repair unstrangulated diaphragmatic hernia, to remove intrathoracic cysts and neoplasms, for exploration or to remove extensive tumors of the wall of the chest should be preceded two or more days by temporary paralysis if after healing the lung can regain its normal volume, or by permanent paralysis if there is to be a reduction in the volume of the lung that will exceed the amount compensatory emphysema can correct.

The reasons are definite. An immobile diaphragm facilitates operation. Reduced volume and excursions of the lung and the consequent increment in unit volumes of blood raise pleuopulmonary resistance to infection several-fold, promote repair and reduce discomforts.

*Wider Application*—Induced transient paralysis has not been employed in combating severe types of traumatic pleuritis, particularly when accompanied by effusion. Induced temporary paralysis has not been utilized in the treatment for pneumonias of the central type, whether bronchial or lobar, which do not provoke sufficient irritation of the visceral pleura to cause reflex inactivation of the diaphragm nor in the treatment for unresolved pneumonia or of incipient pneumonic pleuritis when the diaphragm is not immobile.

Benefits to be obtained under such conditions are not hypothetical, but proved, and exceed the slight discomforts of a simple operation and the temporary reduction in vital capacity which, if it is embarrassing, can be overcome by placing the patients in an oxygen chamber.

#### SUMMARY

Means are available to induce, safely and with little discomfort, transient, temporary or permanent unilateral or bilateral paralyses of the diaphragm which reproduce spontaneous paralyses that are natural protective responses to the more acute pleuopulmonary irritations.

The consequences of the paralysis are both beneficial and detrimental and have been proved experimentally and clinically. The benefits are an increment in pleuopulmonary powers of resistance, defense and repair and in the restriction of dissemination of noxious products, bacteria and tumor cells from inflammatory and neoplastic lesions.

The detriments, a reduction in vital capacity, often little, if at all, beyond that imposed by disease, need only be transient or temporary unless permanent benefits exceed permanent detriments

The earlier paralysis is induced, the greater its immediate and prophylactic value

Temporary paralysis (phrenicectomy) should not be induced if transient paralysis will suffice

Permanent paralysis (phrenicectomy, excision) should be induced only if temporary paralysis has been proved to be inefficacious or would be insufficient to meet requirements

#### CONCLUSIONS

Induced paralysis of the diaphragm is beneficial to patients suffering from a number of pleuropulmonary diseases

It makes thoracotomy and thoracoplasty simpler and safer

Its greatest value, prophylaxis, is attained by early utilization

Experimental and clinical evidence indicates a more frequent, more extended and earlier employment of this minor procedure, but always in conjunction with other measures

# EXPERIMENTAL HEALING OF BONE AFTER PARATHYROIDECTOMY<sup>1</sup>

KELLOGG SPEED, M D

AND

DEAN L RIDER, M D

CHICAGO

As a part of a problem in healing of bone under varying conditions of abnormal blood calcium and phosphorus undertaken by the senior author, the definite results of experimental healing of bone in dogs after parathyroidectomy seem worthy of a separate report

One of the first experiments on the influence of the parathyroids on healing of bone was made by Morel<sup>1</sup> in 1910, this covered the influence of the parathyroids on consolidation of fractured bones in cats, and followed his report of the previous year, which dealt with the action of the parathyroids on the growth of healthy bone His experiments covered, first, ablation of most of the parathyroid tissue in adult cats, which was found not to retard the process of ossification of experimental fractures, second, similar ablation of most of the parathyroid and thyroid tissue in young cats, which resulted in a delay in the healing of the fractures for an average of seven weeks Four cats were used two died, one had tetany, and in the fourth a delayed bony union was demonstrated in comparison with two controls that showed normal union after fracture The process in the thyriparathyroidectomized cats was characterized by a flexible voluminous callus which was almost exclusively cartilaginous Morel referred to Canal's work and asserted that his conclusions verified Canal's, namely, that this operation in cats caused a retardation of bony healing after fracture in young cats only, not in adults After study of this report, the feeling exists that a complete thyriparathyroidectomy was not done on the animals that lived, but that enough parathyroid tissue was removed to verify delayed union after fracture in cats

The influence of parathyroidectomy on bony healing in rats and puppies was investigated by Ogawa, in 1925, from a different angle -

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Submitted for publication, Feb 20, 1930

From the Surgical Department, Rush Medical College

1 Morel, L Compt rend Soc de biol 68 163, 1910, 66 837, 1909

2 Ogawa Healing of Fractures in Reference to the Parathyroids, Arch  
exper Path u Pharmacol 109 83, 1925

He carefully reviewed the literature back to 1896 and believed that the difference in results obtained in these experiments was due to improper removal of the parathyroids, that is, incomplete removal, some of the active glandular tissue remaining. After parathyroidectomy on his animals, he gaged the effect on healing of bone by a chemical analysis



Fig 1—*A*, bones removed from the legs of dog 50, left and right. See table 3. The right leg is shown six weeks after fracture, it has reasonable bony union. The left leg is shown three weeks after fracture, it presents no union, especially in the radius. Considerable amount of callus is formed beneath the periosteum extending up the shaft of both bones of both legs, and yet the amount of callus in the fracture is slight. *B*, bones from the legs of dog 51 (table 3). Only the right leg of this dog was broken, and three weeks have elapsed since the fracture. The scant amount of callus attempt is apparent, although the bones are in excellent apposition. No union is present.

of the callus, estimating its calcium content ( $\text{CaO}_2$ ). He found that if parathyroid extract was given to the animal after experimental fracture, the callus was greater than in normal controls, that is, it contained less water more ash and more calcium. After thyroidectomy alone there was also a greater amount of callus, with no change in the water and ash content, but a slightly greater amount of calcium than in normal controls. He observed that in dogs it was necessary to remove the thyroid also, in order to be sure that all parathyroid tissue was obtained. The conclusion was reached that the parathyroid hormone and the thyroid hormone work antagonistically in the laying down of calcium in callus.

Another interesting series of experiments was performed by Hammett,<sup>3</sup> in whose papers are given the results of a study of the gross anatomy and chemical differentiation of the humerus and femur of the male and female albino rat during their period of growth, from 75 to 150 days of age, and the influence of thyroparathyroidectomy and parathyroidectomy on this growth. The study concerned itself mostly with an ash analysis of the bones with determination of the calcium, magnesium and phosphorus contents. The glandular deficiencies were initiated at 75 days of age.

It was found that in normal bone at 75 days of age the calcium percentage content of the femur is less than that of the humerus in both sexes, there is no discussable difference in the magnesium or the phosphorus contents. During the period from 75 to 100 days of age, there is a definite increase in the calcium percentage of both bones of both sexes, but no shifts in the magnesium or phosphorus percentages. This age difference is directly correlatable with the fact that the rate of growth of the femur in weight and length and in increment of water, organic matter and ash, are greater than that of the humerus during the growth period from 75 to 100 days of age.

The bones of thyroparathyroidectomized rats showed that the percentage of composition of these bones, femur and humerus, was the same, save that in males the phosphorus percentage was greater in the femur than in the humerus. Both these bones of both sexes of the group operated on had less ash, calcium, magnesium and phosphorus. The bones were also lighter and shorter, and contained less water and organic matter. The bone of both sexes of parathyroidectomized rats contained smaller absolute amounts of ash, calcium and phosphorus.

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3 Hammett, F. S. Thyro-parathyroidectomy, *J. Metab. Research* **5** 169 (April-June) 1924, Calcium, Magnesium and Phosphorus Content in Bone Ash of Rats *J. Biol. Chem.* **72** 505 (April) 1927, Chemical Differentiation of Bone During Growth Studies of Thyroid Apparatus, *J. Exper. Biol.* **47** 95 (Feb.) 1927.

In 1927, Stewart and Percival,<sup>4</sup> in their studies of calcium metabolism, especially that on the action of the parathyroid glands in controlling the concentration of the calcium in the blood, observed that the parathyroids may affect the absorption or excretion of calcium or at least exert some controlling action on the equilibrium between the different forms of combination in which calcium exists in the blood and between the concentration in the blood and in the tissues. It was Green-

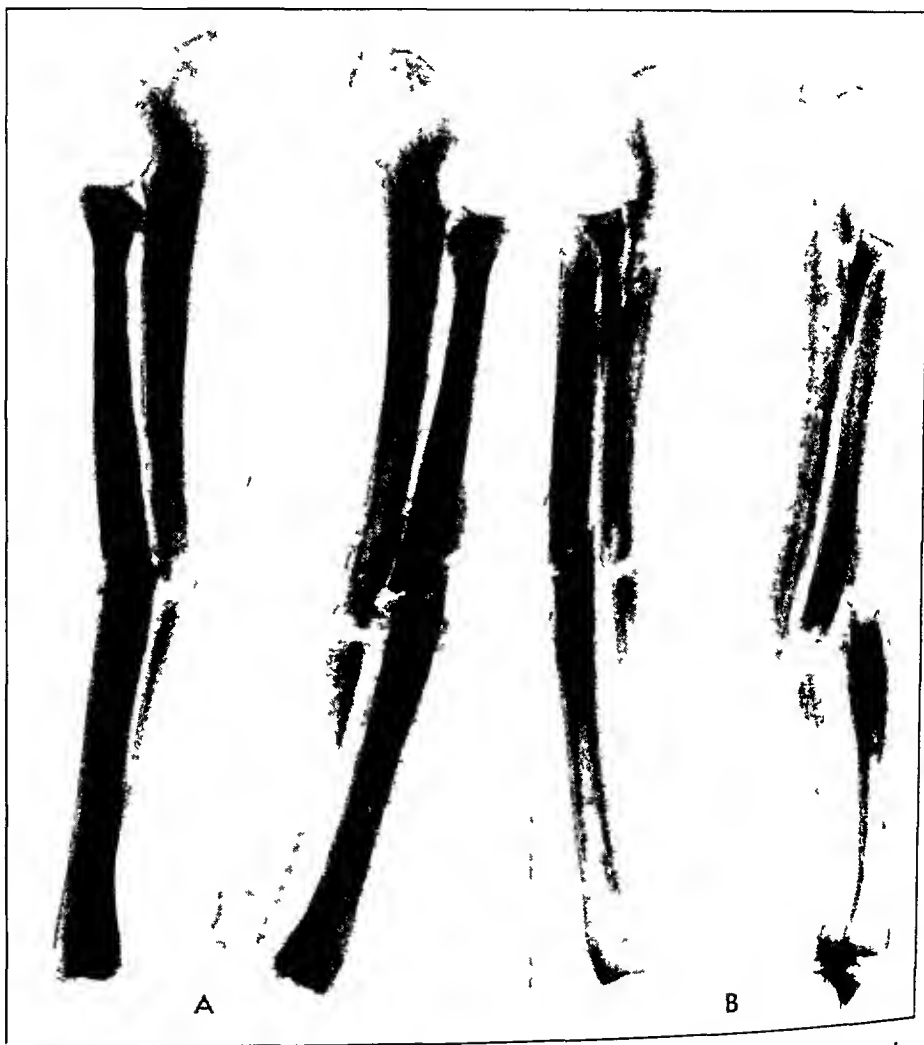


Fig 2—*A*, bones from the legs of dog 53 (table 3). The right leg is shown six weeks, and the left leg, three weeks after fracture. Apposition between the fragments in these fractures is not as complete as in the legs of dogs 50 and 51. There is a scant amount of callus at the site of fracture, even in the six weeks fracture of the right leg, the left leg, three weeks after fracture, shows little callus. Incomplete union is seen in both legs. *B*, bones from the legs of dog 52, the right leg six weeks, and the left three weeks, after fracture. Apposition in the right leg is not as good as in the left leg. There is insufficient amount of callus at the site of fracture, so that nonunion is apparent in both specimens. There is still considerable subperiosteal callus remote from the site of fracture.

<sup>4</sup> Stewart, C. P., and Percival, G. H. Studies in Calcium Metabolism. *Biochem J* 21:301, 1927.

wald and Gross who suggested, in 1925, that the parathyroid hormone is the substance which keeps in solution the large excess of basic calcium phosphate

Stewart and Percival<sup>4</sup> found that in cats repeated hemorrhages (bleedings) did not reduce the proportion of blood calcium. Parathyroid hormone given subcutaneously caused a rise in blood calcium about one-half as fast in cats as in dogs. When it was given intravenously, the action was much quicker. Oral administration of sodium bicarbonate lowered blood calcium, probably by producing a decreased acidity of the intestinal contents, which militates against the absorption of calcium or by bringing about an increased absorption of sodium, thereby causing an alkalosis, which results in a direct lowering of blood calcium. Their experiments show that the parathyroid hormone exerts an influence on the blood calcium content without drawing on external sources of calcium, that is, without stimulating absorption of calcium from the alimentary tract. The increase in serum calcium following the administration of parathyroid hormone is due, then, to the withdrawal of calcium from body tissues, as the increase takes place without any diminution in the excretion of calcium and without possibility of any additional absorption from the alimentary tract.

In efforts to ward off parathyroid tetany, Wade,<sup>5</sup> in 1929 gave animals cod liver oil in amounts up to 50 cc daily for two to three weeks before parathyroidectomy, and he found that while fatal tetany was delayed and the general severity of the tetany was diminished, the blood calcium dropped as much as or even lower than in animals that had not had cod liver oil.

In 1928, Fine and Brown<sup>6</sup> studied the influence of parathyroid extract-Collip<sup>7</sup> on regeneration of bone. They worked with dogs in an effort to study repair of bone under the influence of the extract. They made trephine openings in the femur and found no evidence of difference in regeneration of the bones compared with controls, either in examination by means of the x-rays or in the gross specimen. They also removed ribs subperiosteally, isolating the dogs on a meat and milk diet, and concluded that the parathyroid extract-Collip delayed the speed of deposition of calcium in regenerating bones of young dogs, its action

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<sup>5</sup> Wade, P. A. Calcium and Cholesterol in Relation to Thyroid Parathyroid Apparatus, *Am J M Sc* **177** 79 (June) 1929.

<sup>6</sup> Fine and Brown. Influence of Parathormone on Bone Regenerations, *New England J Med* **198** 932 (June 21) 1928.

<sup>7</sup> Collip, J. B. Therapeutic Value of Parathormone *J A M A* **87** 908 (Sept 18) 1926, Parathyroid Hormone, *J Biol Chem* **63** 395 (March) 1925, Calcium Mobilizing Hormone of Parathyroid Glands, *J A M A* **88** 565 (Feb 19) 1927.



on adult dogs was not ascertained. They believed, consequently, that the use of the extract for delayed bony union was not based on any sound principle.

The healing of fracture in parathyroidectomized albino rats was also investigated by Chandler,<sup>8</sup> who caused a fracture of one bone of the forelimb at the time of parathyroidectomy. Histologic studies of the bones ten, fourteen and twenty-one days after operation were made.

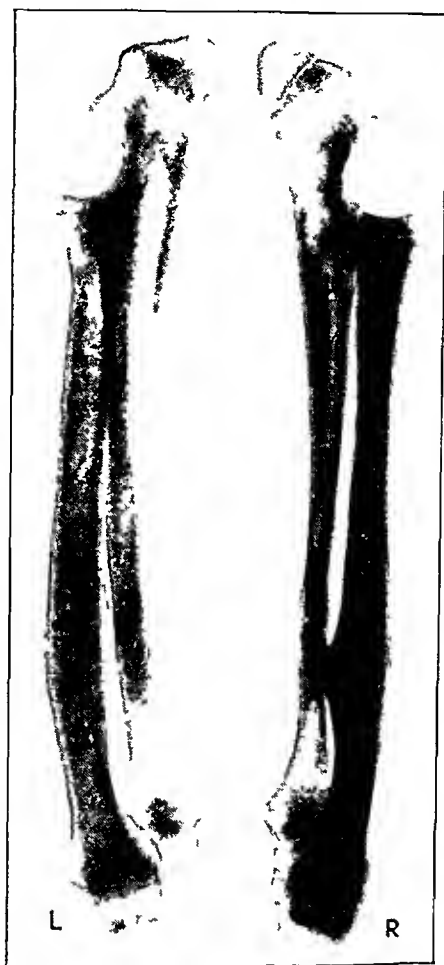


Fig. 3—Bones removed from the legs of an average normal control dog (table 3). The right leg, shown six weeks after fracture, presents firm bony union with solidified callus. The left leg shows a satisfactory bony union with firm callus formation. This represents a normal reaction of a normal dog to such experimental fracture.

Litter mates were used as controls. There was no significant difference in the healing of the bones in the two groups of albino rats.

A clinical assumption after observation on man, that injection of parathyroid extract increases the calcium in the blood, thereby furnishing

<sup>8</sup> Chandler, S. B. The Healing of Fractures in Parathyroidectomized Albino Rats, *Anat. Rec.* **35** 7, 1927.

more calcium for fracture callus has rightly been questioned. Union following administration of the parathyroid extract-Collip in instances of delayed union is not necessarily caused by the injection. Lehman and Cole<sup>9</sup> believed that the issue has been confused, that the action of the parathyroid extract is to mobilize the fixed calcium of the body and that hence it should not offer aid in hastening or inducing a deposit of calcium salts in the soft tissue (callus) about a fracture. They believed that excess callus found after using the parathyroid extract must come largely from the bones themselves. Hunter and Aub, in their study of lead poisoning, found that calcium excretion in patients is rapidly increased in an amount parallel to an increase in the blood serum calcium on the administration of parathyroid extract. If analogy is drawn then between the white rat and man, the level of the blood calcium is not the essential factor on which depends the rate of calcification of callus, as the tendency after injection of parathyroid extract is toward a reduction of the calcium in the bones, and one would expect the withdrawal of calcium from the callus itself and a delay of union.

As a logical sequence to such an argument, Gold<sup>10</sup> discussed the significance of enlargement of the parathyroid gland in osteitis fibrosa generalisata. He found that the literature on this disease, Paget's disease and osteomalacia often mentioned associated parathyroid enlargement. Of seventeen cases of parathyroid enlargement studied at autopsy by Maresch of Vienna, thirteen gave evidence of skeletal changes. In six instances in this group, osteomalacia had been diagnosed, in five, osteitis fibrosa, in one, osteoporosis, and in one, Paget's disease.

Gold reported the case of a woman, aged 54, who had osteitis fibrosa cystica. A tumor of the right superior parathyroid was found and extirpated. Six months after operation there was improvement clinically, chemically and roentgenologically. The blood calcium dropped from 30 per cent plus to normal. The previous abnormal excretion of calcium in the urine also approached normal. Microscopic examination of the gland showed a benign adenoma.

Ross<sup>11</sup> said that he had repeated the experiments of Moel<sup>1</sup> Ogawa<sup>2</sup> and others, using improved precautions, in a study of the effects of excision of different amounts of the four parathyroid glands in cats. He verified the condition of the experimental fractures at different intervals by roentgenologic examination and determined the blood calcium content during this course of time.

<sup>9</sup> Lehman, E. P., and Cole, W. H. Parathyroid Hormone and Calcification, *J. A. M. A.* **89** 587 (Aug. 20) 1927.

<sup>10</sup> Gold, Ernst. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **41** 63, 1928.

<sup>11</sup> Ross, D. E. Relation of the Parathyroids to the Healing of a Fracture as Controlled by the Roentgen Rays, *Arch. Surg.* **16** 922 (April) 1928.

The phosphorus content of the blood was determined both before and after the removal of two or three parathyroid glands, but no change in the phosphorus level was found. In the first five or six days following fracture in a normal cat, an invasion of the blood clot at the site of fracture by fibrous connective tissue was found. By the tenth or eleventh day, the blood clot had almost entirely disappeared and was replaced by connective tissue, with a small amount of cartilage and a



Fig 4—Photomicrograph of the right leg of an average normal dog six weeks after fracture,  $\times 366$ . See table 4. There is abundant callus with calcified bony trabeculae almost hiding the site of the fracture. The medullary cavity is not yet established through the site of fracture.

few small areas of bone. This invasion of blood clot by connective tissue and the formation of cartilage occur in cats from which three parathyroids have been removed. The process of bony union after that stage is delayed. Ross concluded that removal of two parathyroids does not (in cats) delay union of a fracture, removal of three parathyroid-

delays union for as long as from four to five weeks. The excision of two parathyroids does not diminish the blood calcium, but excision of three causes a drop of from 2 to 3 mg of serum calcium per hundred cubic centimeters. When the blood calcium returns to a normal level, bony union of these experimental fractures follows. Removal of two or three parathyroids does not influence the blood phosphorus level, and a certain amount of mobility at the site of fracture is not deleterious to bony union.

In the experiments on dogs here reported, Scholz' dictum that the untreated cretin retains phosphorus and excretes an abnormal amount of alkaline earths was borne in mind, and thyroid was given to the thyro-parathyroidectomized dogs in doses of 3 grains (0.18 Gm) per diem, because it was felt that the administration of this thyroid exerted no influence on the phosphorus metabolism, but reduced the urinary excretion of alkaline earths, particularly calcium, and thereby influenced tetany favorably. A confirmation of this fact was noted by Aub, Bauer, Heath and Ropes, who noticed that the increase of calcium excretion in exophthalmic goiter is out of proportion to the basal metabolism, e. g., a basal metabolic rate of 55 plus gave a calcium excretion of 170 per cent above normal. Similarly, in six patients with myxedema it was found by them that the average excretion of calcium was 40 per cent below normal. Without any change in dietary intake, feeding thyroid to these patients resulted in an increase in both metabolism and calcium excretion, verifying the point that the thyroid extract acts to increase the endogenous calcium metabolism while the extra elimination of calcium comes from the tissues, presumably mostly from the bones. In two instances of parathyroid tetany with low calcium levels in both blood and excreta, the response to thyroid therapy was shown by a distinct elevation not only of the calcium excretion but also of the serum level. Aub, Bauer, Heath and Ropes considered that the effect of thyroid secretion on calcium excretion is greater than its effect on total metabolism. Probably the effect of thyroid is merely a direct catabolic action on the calcium deposits in the bones, although the high rate of calcium elimination is not found in the blood itself.

This reserve or easily influenced supply of calcium may be in cancellous bone. Bauer, Aub and Albright<sup>12</sup> noted that the amount of cancellous bone varies in different animals, and they concluded after their studies that the bone trabeculae of cancellous bone are early depleted by prolonged administration of parathyroid extract-Collip, that a long-continued high calcium diet results in a rapid accumulation of

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<sup>12</sup> Bauer, Aub, and Albright. Calcium and Phosphorus Metabolism, Bone Trabeculae as Source of Calcium. *J. Exper. Med.* **49**: 145 (Jan. 10) 1929, *Quart. J. Med.* **20**: 123, 1926-1927.

trabeculae and that bone trabeculae serve as a storehouse of readily available calcium, whereas the shafts of bones undergo a slow progressive exchange of inorganic salts and are not influenced, except in case of unusual body demands

One theory might be advanced in the consideration of the physics of bone, namely, that the calcium in bones is divided into two parts, a



Fig 5—Photomicrograph of left leg of an average normal dog three weeks after fracture,  $\times 366$ . The union is satisfactory, with calcified cartilage present and every evidence of bony union to follow. See table 4

larger portion making up the solid structural part of the bone, which functions primarily as a mechanism for body support, and a smaller less stable or more easily influenced portion lying in the trabeculae or cancellous bone and acting as a ready reserve for use when body requirements demand calcium salts. The anatomic situation of the trabeculae according with this theory, the trabeculae are most numerous where the blood



Fig 6—Photomicrograph of right leg of dog 50 six weeks after fracture. This dog had had a thyroparathyroidectomy. In table 4, a description of this section is available. There is much uncalcified callus with connective tissue and fat cells, but no mature bone is present.



Fig 7—The left leg of dog 50 which had undergone a thyroparathyroidectomy. No mature bone is present and nonunion is still seen. Consult table 4 for more details.

supply is greatest. The delicate bone trabeculae in close relationship to the bone-marrow are well situated to receive calcium deposits in times of calcium excess and to give up calcium in times of need.

The results obtained from the experimental work on dogs are explained in tables 1, 2, 3 and 4.

Table 1 shows the average determinations of serum calcium and phosphorus per hundred cubic centimeters in adult dogs.

Table 2 shows the clinical course of four dogs which, out of ten survived thyroparathyroidectomy and the subsequent tetany and other mishaps and were subjected to experimental fracture. All dogs were kept in separate cages, mostly in an isolated part of the laboratory, and

TABLE 1—*Determinations of Blood Calcium and Phosphorus in Dogs After Parathyroidectomy*

Dog 50, on Which Thyroparathyroidectomy Was Performed, April 17, 1929*	Calcium, per 100 Cc	Phosphorus, per 100 Cc	Diet	Weight, Kg
April 16, 1929	10.2	3.8	Normal	13.6
April 23, 1929	6.3	5.8	Normal	14.0
May 10, 1929	7.0	5.9	Normal	14.5
May 23, 1929	6.9	7.0	Normal	15.0
June 1, 1929	6.3	7.4	Normal	15.2
June 14, 1929	6.5	7.8	Normal	14.5
June 26, 1929	6.8	7.8	Normal	13.9
July 4, 1929	6.5	8.2	Normal	12.8
July 11, 1929	6.1	10.0	Normal	11.9
July 12, 1929	6.1	9.4	Normal	
Twenty normal dogs averaged	10.1	6.0		

\* All dogs conformed more or less exactly to dog 50 in respect to these observations.

watched for tetany. Only the most assiduous attention and quick efforts made it possible to bring four dogs through to the point of fracture. It was found that these dogs after recovery from tetany did not take ether well. The fractures were induced by a Thomas wrench, and the leg involved was immediately enclosed in a circular plaster dressing. These dressings had to be renewed in several instances, and there was some movement at the site of fracture on some weight bearing when the dog got up. Several normal dogs, some litter mates, were used as controls.

Table 3 shows the results of clinical and roentgenologic examinations for the evidence of bony union in the four thyroparathyroidectomized dogs subjected to fracture.

Table 4 shows the microscopic evidence of healing of bone in the fractured legs of these four dogs, compared with that in the average normal dog.

TABLE 2—*Clinical History of Dogs Subjected to Fracture After Parathyroidectomy*

Dog	Operation	Postoperative Treatment	Fracture	Postfracture Course	Fracture	Postfracture Course	Death
50	4/17/29, thyro para thyroid ectomy	Calcium lactate 15 grain per kilogram of weight per diem in 3 parts discontinued, 5/18/29	5/23/29, right leg, under ether	Tetany, return to calcium 6/16/29, 3 grains thyroid daily 6/17/29, attempted to walk	6/20/29, left leg, under ether	No tetany, depressed, calcium lactate no influence, 6/29/29, improved	7/11/29, in tetany autopsy no thyro para thyroid tissue
51	5/6/29, thyro para thyroid ectomy	Calcium gluconate in vein, thyroid removed, calcium lactate by stomach tube discontinued, 5/21/29	6/1/29, right leg, under ether	Thyroid feeding, depressed 6/11/29, tetany calcium lactate renewed			6/20/29, in tetany autopsy no thyro para thyroid tissue
53	6/8/29, thyro para thyroid ectomy	Thyroid removed calcium lactate, 6/10/29 to 6/18/29	6/20/29, right leg, under ether	Depressed, calcium lactate therapy no help, no attempt to use leg	7/13/29, left leg, under ether	Not much attempt to use legs as right leg, not strong, few steps 7/27/29 to 8/1/29 on both legs	8/1/29, no thyro para thyroid tissue
52	6/14/29, thyro para thyroid ectomy	Thyroid removed, calcium lactate, 6/17/29 to 6/24/29	6/27/29, right leg, under ether	Good condition, 7/2/29, attempted to use leg	7/18/29, left leg, under ether	Lay in cage, began to walk 8/1/29	8/8/29 killed, no thyro para thyroid tissue
Normal Control Dog (example of several dogs)							
	Normal dog, blood calcium 9.8 to 6, blood phosphate 5.2 to 4	No glandular operation no medication	2/28/29, right leg, under ether	Not much weight on leg first week, seemed to have pain in it when walking until 3/18/29, then normal, no limp, cast off 3/20/29	3/21/29, left leg, under ether	Recovery slow, depressed 1 week, by 4/5/29 walking without limp	4/10/29, killed

TABLE 3—*Results of Clinical and Roentgenologic Examination for Evidence of Healing of Bone in Dogs After Parathyroidectomy*

Dog	Clinical Examination		Examination by Means of X Rays	
	Right Leg	Left Leg	Right Leg	Left Leg
50	At 6 weeks, bony union	At 3 weeks, small callus motion at site of fracture	At 6 weeks, bony union	At 3 weeks, small callus, nonunion in radius
51	At 3 weeks, no union, motion between fragments		At 3 weeks, little callus, fracture still looks recent	
53	At 6 weeks, callus apparent, especially in radius crepitus when moved union firm, except in lateral plane	At 3 weeks, callus apparent, some bending, slight motion in both bones	At 6 weeks, callus good, denser on radius firm bony union ulna less dense but more so than 3 weeks' specimen	At 3 weeks, fair callus both bones, greater in radius, which appears completely united ulna, clear space between incomplete union
52	At 6 weeks callus apparent false motion both bones slight crepitus	At 3 weeks, callus around radius, little around ulna false motion at site of fracture no inclusion of soft parts	At 6 weeks, mal apposition of fragments apparent callus especially in distal fragments true nonunion most of callus subperiosteal not around fracture	At 3 weeks apposition good, more callus around radius, subperiosteal not in plane of fracture no union present
Normal Control Dog (example of several dogs)				
	At 6 weeks firm bony union	At 3 weeks firm bony union	At 6 weeks firm bony union	At 3 weeks firm bony union



TABLE 4—*Results of Microscopic Examination of Experimental Bone Healing After Parathyroidectomy*

	Three Weeks After Fracture	Six Weeks After Fracture
Dog 10 (normal control)	Abundant network of trabeculae along fracture plane, small islands of calcified cartilage surrounding small spicules of necrotic bone, islands surrounded by osteoid tissue, around periphery, partly calcified cellular tissue with large bone cells and some old hemorrhages	Abundant network calcified bony trabeculae fills cavity of bone marrow and extends on outside of shaft for 20 mm, thickness, 3 mm, spaces between trabeculae filled by vascular cellular connective tissue
Dog 50 (parathyroid removed)	Much uncalcified callus, out of which develop branches trabeculae of osteoid tissue which surrounds poorly calcified islands of callus, in spaces between trabeculae are fibrillar connective tissue and fat cells, no mature bone	Irregular structureless masses of calcium salts arranged perpendicularly to surface of bone, these masses surrounded by uncalcified callus, formed of trabeculae, spaces between trabeculae contain connective tissue and fat
Dog 51 (parathyroid removed)	No newly formed tissue along fracture plane, on outside is bridge of small amount of callus surrounded by old blood, slender osteophytes about the intact bone, no bony union	
Dog 53 (parathyroid removed)	Callus tissue, smaller amount of osteoid tissue than in 3 week stage of dog 50	Histology identical with that of six week specimen of dog 50
Dog 52 (parathyroid removed)	Fracture bridged on outside by callus, no union in plane of fracture	Histology corresponds to that of same period of dog 50, except central deposits of calcium are less extensive, no bony union

### CONCLUSIONS

A study of serum calcium alone in dogs would show merely the height of the calcium stream or balance, it would not give any indication as to the direction of its flow, whether into excretory channels or into the bones. On these parathyroidectomized dogs in which tetany was controlled by the use of calcium lactate and thyroid extract, no determinations of the calcium content of the excreta were made. The lack of calcification of the bones after experimental fracture, in conjunction with the low blood calcium led to the inference that the calcium stream was directed away from the bones after parathyroidectomy, and that parathyroidectomy, either through this change of calcium stream or balance or through some still undiscovered factor, delays the healing of fracture in experimental dogs.

# A COMPARISON OF THE EFFECTS OF HEMORRHAGE UNDER ETHER ANESTHESIA AND UNDER SPINAL ANESTHESIA \*

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Owing to the frequent employment of spinal anesthesia in recent years, a clearer understanding of its effect on the general circulation seems important. Occasional deaths following its use have been unexplained. Recently, we had occasion to observe a patient who died following the termination of an operation under spinal anesthesia. During the operation approximately 250 cc of blood was lost. As no other cause for the patient's death was found, it was believed that the hemorrhage probably was responsible for it. The loss of this amount of blood in an adult patient under ether anesthesia does not usually produce deleterious effects.

The purpose of the present study is to determine the effects of loss of blood under ether anesthesia and under spinal anesthesia.

## METHODS

Dogs were used in all experiments. The blood pressure level was determined by placing in the carotid artery a cannula which was connected to a mercury manometer. The cardiac output was calculated from the Fick formula:

$$\frac{\text{Cc oxygen consumed per minute}}{\text{Cc oxygen taken up by 1 cc of blood in passing through the lungs}} = \frac{\text{Cc of blood passing through the lungs per minute}}{\text{Cc of blood passing through the lungs per minute}}$$

The animals were bled from a cannula placed in either the femoral or the carotid artery.

In the experiments in which the effects of hemorrhage during ether anesthesia were determined, the animals were anesthetized by ether for periods of time varying from one hour and thirty-seven minutes to two hours and thirty-seven minutes before the initial bleeding. The anesthesia was profound in all instances. At the end of this period, the cardiac output and the blood pressure were determined. At five minute intervals, until the animal had been bled from three to six times in the different experiments, an amount of blood was removed at each bleeding which equaled in most instances 5 cc per kilogram of body weight. Five minutes after the last removal of blood, the cardiac output and blood pressure were again determined, and the experiment was discontinued.

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\* Submitted for publication Feb 2, 1930

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In the experiments in which the effects of hemorrhage during spinal anesthesia were determined, barbital or morphine in amounts sufficient to permit the introduction of cannulas was given. A solution of procaine hydrochloride (1 per cent) and strychnine sulphate (0.1 per cent) was used in some experiments and procaine hydrochloride (1 per cent) in others. From 0.3 to 1 cc of the fluid was injected into the spinal canal in the lumbar region. The animal was placed on its side for the introduction of the anesthetic and was then changed to the dorsal position. The board on which the animal was lying was at all times kept parallel to the floor. After the needle was introduced into the spinal canal, several drops of the spinal fluid were withdrawn into the syringe and reinjected with the procaine and strychnine sulphate solution. After periods of time varying from twenty to forty-seven minutes after the solution was injected, the cardiac output and blood pressure were determined. The blood was then removed from the animal usually at five minute intervals, the total amount removed varying in the different experiments from 8 to 30 cc per kilogram. In most instances the individual bleedings were of approximately the same size as those in the experiments performed under ether anesthesia. After the last bleeding an attempt was again made to determine the cardiac output and blood pressure.

### RESULTS

The cardiac output and blood pressure were not determined before the ether was administered. A comparison of the figures that were obtained after the animals had been anesthetized for varying intervals of time with those of similar figures on normal unanesthetized animals shows that the ether anesthesia did not alter markedly the cardiac output and blood pressure. Two of the four dogs were bled 0.5 per cent of the body weight at five minute intervals until 3 per cent had been removed. Determinations of the cardiac output and blood pressure after the last bleeding showed a marked decline as compared with that before the first bleeding but the animals were in no grave danger of immediate death. Removal of blood amounting to 1.5 per cent of the body weight caused some reduction in the cardiac output and blood pressure but spontaneous recovery of the animal undoubtedly would have taken place had the anesthetic been discontinued. The results of the experiments in which ether anesthesia was used are given in table 1.

In an attempt to determine whether or not ether anesthesia increases the danger of circulatory failure from hemorrhage, two animals were bled 0.5 per cent of the body weight at five minute intervals. No anesthetic was used except procaine hydrochloride which was injected at the site of the introduction of the cannula. The reaction of the animal to hemorrhage was approximately the same as that in the animals which were anesthetized by ether. As it has already been shown (Blalock and Harrison<sup>1</sup>) that normal dogs do not reach a state of severe shock until

1 Blalock, A., and Harrison, T. R. The Regulation of Circulation. V. The Effect of Anemia and Hemorrhage on the Cardiac Output of Dogs, *Am J Physiol* 80: 157, 1927.

TABLE 1—*Effects of Hemorrhage During Ether Anesthesia*

Experiment	Weight, kg	Before Bleeding		After Last Bleeding		Time Interval Between Beginning Anesthetic and Bleeding	Bled, Cc per kg	Total Amount Bled, Cc per kg
		Cardiac Output, Cc per Minute	Mean Blood Pressure, Mm of Mercury	Cardiac Output, Cc per Minute	Mean Blood Pressure, Mm of Mercury			
1	15.5	2,000	127	710	32	{ 1 hr 37 min 1 hr 42 min 1 hr 47 min 1 hr 52 min 1 hr 57 min 2 hr 2 min	{ 5 5 5 5 5 5	30
2	11.5	1,480	122	490	28	{ 1 hr 46 min 1 hr 51 min 1 hr 56 min 2 hr 1 min 2 hr 6 min 2 hr 11 min	{ 5 5 5 5 5 5	30
3	12.0	3,132	124	2,448	120	{ 2 hr 26 min 2 hr 31 min 2 hr 36 min	{ 5 5 5	15
4	11.3	2,456	105	1,235	50	{ 2 hr 37 min 2 hr 42 min 2 hr 47 min 2 hr 52 min	{ 4 4 4 4	16

TABLE 2—*Effects of Hemorrhage During Spinal Anesthesia*

Experiment	Weight, kg	Before Bleeding		After Final Bleeding		Time Interval Between Spinal Anesthetic and Bleeding	Bled, Cc per kg	Total Amount Bled, Cc per kg
		Cardiac Output, Cc per Minute	Mean Blood Pressure, Mm of Mercury	Cardiac Output, Cc per Minute	Mean Blood Pressure, Mm of Mercury			
1	10.0	420	34	0	0 (died)	{ 25 minutes 30 minutes 35 minutes 40 minutes	{ 4 4 4 4	16
2	12.3	800	34	0	0 (died)	{ 25 minutes 30 minutes	{ 4 4	8
3	13.6	660	46	0	0 (died)	{ 40 minutes 50 minutes	{ 4 4	8
4	11.8	1,340	66	420	28	{ 45 minutes 40 minutes 45 minutes 50 minutes	{ 4 4 4 4	16
5	9.0	2,530	95	450	40	{ 25 minutes 30 minutes 35 minutes 40 minutes 45 minutes 50 minutes	{ 5 5 5 5 5 5	30
6	11.4	2,100	70	365	16	{ 20 minutes 25 minutes 30 minutes	{ 5 5 5	15
7	13.6	2,230	66	0	0 (died)	{ 13 minutes 25 minutes	{ 6 6	12
8	16.8	2,540	110	1,010	32	{ 1 hr 47 min 1 hr 25 min 1 hr 55 min	{ 11 7 9	27
9	14.1	1,580	28	950	24	25 minutes	9	9

blood amounting to 3 or 4 per cent of the body weight has been removed, further observation on normal dogs seems unnecessary at the present time

The effects of hemorrhage during spinal anesthesia were determined in nine experiments. The blood pressure and cardiac output before the initial bleeding were usually at a lower level than those found in normal animals. In four of the nine animals, death was produced by removing an amount of blood which varied from 0.8 to 1.6 per cent of the body weight. In at least two of the five remaining experiments the cardiac output and blood pressure were reduced much more than would have been anticipated had ether anesthesia been employed. The results of these experiments are given in table 2

#### COMMENT

It has been stated by previous workers that spinal anesthesia causes a decline in blood pressure unless its administration is accompanied by the giving of a vasoconstrictor drug such as ephedrine or epinephrine. Burch and Harrison<sup>2</sup> have found that the output of the heart is also diminished, but the decline is usually not as relatively great as is the decline in blood pressure. In these experiments different dogs varied greatly as to the amount of blood loss which could be tolerated under spinal anesthesia. Two of the nine animals withstood a loss of blood amounting to approximately 3 per cent of the body weight without producing death. This difference is probably due to the fact that spinal anesthesia causes a greater reduction in blood pressure in some animals than in others. It has been noted that there is a great individual variation in the effects of spinal anesthesia on the blood pressure of patients.

Cattell<sup>3</sup> studied the effects of administering ether to dogs which had been bled from 15 to 20 per cent of the estimated blood volume and found that a decline in blood pressure usually resulted. It was thought that the decline in blood pressure was due to a reduction in the cardiac output. In other experiments, Cattell noted that ether administered after hemorrhage actually increased the blood pressure. Blalock<sup>4</sup> found that ether increases the output of the heart and causes very little alteration in the blood pressure. In the present experiments, comparison of the

<sup>2</sup> Burch, J. C., and Harrison, T. R. The Effect of Spinal Anesthesia on the Cardiac Output, *Arch Surg* **21** 330 (Aug.) 1930

<sup>3</sup> Cattell, McKen. Studies in Experimental Traumatic Shock. VI. The Action of Ether on the Circulation in Traumatic Shock, *Arch Surg* **6** 41 (Jan) 1923

<sup>4</sup> Blalock, Alfred. Cardiac Output in the Dog During Ether Anesthesia. I. The Effect of Ether Anesthesia on the Cardiac Output, *Arch Surg* **14** 72 (March) 1927

effects of hemorrhage during ether anesthesia with the effects of hemorrhage without anesthesia shows that there is very little difference between the two

Spinal anesthesia is contraindicated in patients who have lost a great deal of blood or in patients in whom severe blood loss during the operation is anticipated. This precaution is important if the anesthesia is to extend high enough to produce a marked decline in blood pressure. Spinal anesthesia is especially indicated in patients who have diseases that are associated with an unusually large blood volume or in patients with a high blood pressure.

#### SUMMARY

In dogs, the danger of circulatory failure from hemorrhage is greater under spinal anesthesia than under ether anesthesia.

# EVIDENCE SHOWN IN ROENTGENOGRAMS OF CHANGES IN THE VASCULAR TREE FOLLOWING EXPERI- MENTAL SYMPATHETIC GANGLIONECTOMY\*

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The constant changes that follow sympathetic ganglionectomy and ramisection have been attributed clinically to the increased flow of blood to the extremities, as shown by studies with the calorimeter and the thermocouple, but these conclusions have been based only on physiologic observations. In order to investigate the possibility of establishing an anatomic basis for the explanation of clinical results in such conditions as Raynaud's disease, thrombo-angitis obliterans and polyarthritis, lumbar sympathetic ganglionectomy and ramisection was performed on animals.

Following operation, an opaque medium was injected into the arterial tree, and the arterial tree was then studied by means of the roentgen ray. In view of the fact that the animal on which the experiment could be conducted successfully must necessarily be one that could withstand an anesthetic and be of sufficient size to demonstrate any gross changes in the caliber of the vessels, dogs were chosen. In order that the conclusions should be absolutely unbiased, one of us (Craig) performed the operation, removing the sympathetic ganglions and severing the ramus on one side only, this was done on three animals, then the other investigator (Horton) made the injections. Series of roentgenograms were made after each injection, and the plates were studied. As a check on the operative procedure, the lumbar sympathetic chain was dissected afterward.

## EXPERIMENTAL WORK

On Jan 18, 1929, three dogs were operated on under ether anesthesia. The surgical procedure was practically the same on all three. The technic of Adson, consisting of the transabdominal exposure of the lumbar sympathetic ganglions, was used. Because the ganglions proved to be farther apart in the dog than in man, only two ganglions, the second and third lumbar ganglions and connecting ramus, were resected.

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\* Submitted for publication, Aug 2, 1929

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In the first dog, the second and third lumbar ganglions on the left side were resected, and the lumbar ganglions on the right side were not disturbed. In the second dog, the second and third lumbar ganglions on the right side were resected, and the lumbar ganglions on the left side were not disturbed. In the third dog, the second and third lumbar ganglions on the left side were resected and the lumbar ganglions on the right side were not disturbed. The dogs were then allowed to recover and the injections were not carried out immediately, as we wished to observe the time element in connection with these procedures.

At intervals of twenty-eight, fifty-nine and one hundred and ten days after operation, under ether anesthesia the abdomens of the dogs were

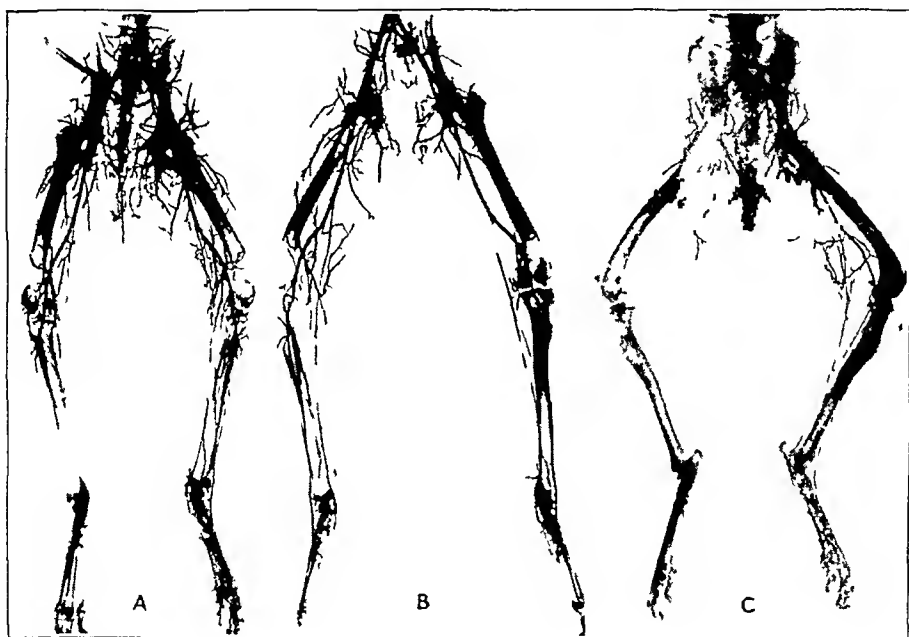


Fig 1—*A*, the second and third lumbar sympathetic ganglions on the left side were removed. Metallic mercury was injected into the arterial tree, a marked difference is shown in the appearance of the two extremities (first dog). *B*, the second and third lumbar sympathetic ganglions on the right side were removed. Metallic mercury was injected into the arterial tree. A slight but definite difference in the appearance of the two extremities may be noted (second dog). *C*, the second and third lumbar sympathetic ganglions on the left side were removed. Metallic mercury was injected into the arterial tree, a marked difference is shown in the appearance of the two extremities (third dog).

opened and a large-sized vessel was incised, allowing the animal to bleed to death. Immediately after death, the dogs were placed on the roentgen-ray table, and with a cannula in the abdominal aorta at the level of the first lumbar vertebra, metallic mercury was injected. Special care was taken to place the animal on the back in a horizontal posi-



tion, with the legs extended so that both knees were equidistant above the table. This enabled the pressure of the injection medium to be maintained at a constant level throughout the entire procedure. The mercury was allowed to flow into the aorta under its own weight, and the dogs were not disturbed until a series of stereoscopic plates had been exposed after varying quantities of mercury had been injected. Following the injection, sections of the arteries were taken for microscopic study.



Fig. 2—Periarterial sympathetic neurectomy was carried out on the left femoral artery, and mercury was injected into the arterial tree. The filling of the arterial tree in both lower extremities is uniform (fourth dog).

Since there has been some controversy in the literature regarding the relative efficacy of periarterial sympathetic neurectomy and lumbar sympathetic ganglionectomy and ramisectomy, another anatomic experiment was carried out to compare the results.

On May 16, 1929, periarterial sympathetic neurectomy was done on a dog, and the outer sheath of the left femoral artery was stripped for 5 cm. Twenty-two days later, the dog was killed and mercury injected into the arterial tree as in the other animals.

It is obvious that there is a definite change in the arterial tree in the extremity to which the sympathetic innervation had been interrupted by unilateral lumbar sympathetic ganglionectomy and ramisectomy (fig 1). This change was not observed in unilateral periarterial sympathectomy, as evidenced by figure 2. When the pressure on the injection mass in the third dog in the series was increased (fig 1c), the injected material filled the arterial tree in both lower extremities (fig 3). The same results were obtained in the first and second dogs.



Fig 3—Mercury injected into the arterial tree under 25 mm of pressure (third dog)

#### SUMMARY

In dogs, definite evidences of vasodilatation in the arterial tree of the hind extremity were observed following interruption of sympathetic innervation by lumbar sympathetic ganglionectomy and ramisectomy. Changes were not observed in the arterial tree following periarterial sympathetic neurectomy. These observations are in accord with the clinical observations in man that have been made at the Mayo Clinic.

# FORTY-SECOND REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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(Concluded from p 554)

## MISCELLANEOUS

*Charcot's Arthropathy*—Wile and Butler<sup>32</sup> analyzed the records and physical observations in eighty-eight patients affected with Charcot's arthropathy, and came to the following conclusions

The greatest age incidence was between 35 and 55 years. In the majority of cases the onset was gradual and insidious and extended over a period of months or years. The occasional sudden production of the condition was frequently the result of trauma bringing into visibility a preexisting subclinical process. The condition occurred three times more frequently in men than in women as compared with the incidence of tabes. Polyarticular involvement was common, no joint in the body being immune, but involvement of the knees and ankles occurred far more commonly than did any other form. Cerebrospinal syphilis was present in the majority of cases. Its absence, however, in typical cases indicated that it was not the essential primary etiologic factor. When present, the form of involvement was more commonly tabes. In the

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32 Wile, U J, and Butler, M G. A Critical Survey of Charcot's Arthropathy, J A M A 94 1053 (April 5) 1930

majority of cases the typical syndrome seemed to be an inactive or arrested cerebrospinal syphilis, few symptoms referable to the syphilis being ordinarily present. Subclinical insults, such as faulty posture and ataxia, played a larger rôle than did the actual trauma antedating the condition. The loss of the afferent nerve paths to the joint, rendering it unable to compensate for injury, seemed to be the ultimate etiologic factor.

*Cystic Bursal Hygromas*—Jones<sup>33</sup> made a study of bursal hygromas, using the records and pathologic observations in fifty-five patients treated for this condition at the Mayo Clinic. He concluded that trauma either severe or represented by a mild continued irritation, was the chief causal factor. He found no evidence to support the theory of infectious origin. The liquid contents of the cysts were partly of degenerative and partly of transudative origin.

Studies of the end-results were made in twenty-seven of the patients. In none had there been any recurrence following excision, which was the treatment advised. The author found a striking similarity between the bursal hygromas and carpal ganglions in their development.

*Joint Complications in Smallpox*—Lombard<sup>34</sup> related two observations of joint sequelae in smallpox, the process in each case taking the form of osteo-arthritis. The first patient was a boy, aged 4 years, in whom during an illness with smallpox, swelling of the elbows developed later followed by suppuration and complete bilateral ankylosis. The second patient presented multiple osteo-articular lesions consecutive to smallpox at the age of 2 years. The hand was deviated to the radial side as a result of destruction of the epiphyseal cartilage of the radius, and in addition there were lesions of the femoral condyles and of the lower end of the tibia. The infection had a tendency to localize in the juxta-epiphyseal regions and apparently had a great affinity for the radius.

*Primary Bone Infection of Mycotic Origin*—Three instances of primary mycotic infection of the bones were reported by Meyer<sup>35</sup>. One patient was a boy aged 12 with symmetrical foci in both os calcis, the second was a youth, aged 19, with a lesion in the outer side of the os calcis. In both cases the organism was *Hemyspora*. The third patient was a youth, aged 16, with a lesion in the upper end of the tibia caused by actinomycosis. In all the patients the first diagnosis had been tuberculosis, and general antituberculous treatment had been instituted without success. Local and general treatment with iodine seemed to have given good results.

33 Jones, H. T. J. Bone & Joint Surg. **12** 46, 1930.

34 Lombard, P. Rev. d'orthop. **16** 490, 1929.

35 Meyer, M. Rev. d'orthop. **16** 624, 1929.

[ED NOTE—Other authors have drawn attention to mycotic infection of bone, and it is evidently a condition to be borne in mind when puzzling lesions are encountered in the bones]

*Study of Joint Fluids*—Kling made a series of studies of joint fluids and reported the results in separate papers

One investigation<sup>36</sup> dealt with the cytology of the fluid in traumatic effusion of the knee. By this means, Kling felt that he had been able to establish fairly conclusively the differential diagnosis between slight injuries to the joint without tear of important ligaments, more severe injuries with tearing of the semilunar cartilages or crucial ligaments and intra-articular fracture. The finding of erythroblasts and myelocytes, both products of bone-marrow, pointed to an intra-articular fracture. This diagnostic indication was verified in some instances when the roentgenograms were negative. When there were only ligamentous tears, fat, blood corpuscles and serum were present in the fluid, while with less severe injuries, such as bursitis and synovitis, only blood corpuscles and serum were found.

In another investigation Kling<sup>37</sup> applied the icterus index test of van den Bergh to effusions of the joint. The local formation of bilirubin raised the icterus index in traumatic hemorrhagic effusions above the level of the blood serum, while in inflammatory effusions the icteric index of the joint fluid was equal to or below the blood serum. In fractures of the joint the icterus index was unusually high. The author believed that this test, which is simple, might be helpful in the diagnosis of diseases of the joints.

In a third investigation, Kling<sup>38</sup> made a comparative study of the Wassermann reaction of the blood and the joint fluids in thirty-five patients. He found that the Wassermann test gave identical results in both the blood and the joint fluids, the joint effusions being chiefly of traumatic origin. The technic of the Wassermann reaction was the same in the joint fluids as in the blood, and he felt that both diagnostic and therapeutic considerations urged the application of the test to the joint fluid in every instance.

*The Histologic Study of Normal and Diseased Bone*—Morrell<sup>39</sup> described a microtome knife that he had devised, made from an alloy of tungsten carbide and cobalt called "widia." With this knife he was able to cut sections varying from 6 to 12 microns in thickness from bone.

36 Kling, D. H. *Am J Surg* 7:824, 1929.

37 Kling, D. H. Bilirubin in Effusions of Joints, *Arch Surg* 20:17 (Jan) 1930.

38 Kling, D. H. *Am J Syph* 13:596, 1929.

39 Morrell, A. H. Untreated Human Bone Sectioned with a New Knife, *Arch Path* 8:816 (Nov) 1929.

immediately after its removal during an operation and without any preliminary treatment. He believed that by the use of this knife the microscopic study and microchemical analysis of bone could be approached in a manner heretofore impossible and with greatly increased possibilities of success.

Jaffe<sup>40</sup> described methods of preparing bone for histologic study for every purpose, that were tried procedures. The choice of the method depended on the purpose of the examination. Unfortunately, there was no method of decalcifying bone that did not injure to a certain extent the cellular elements, the most essential part from the standpoint of a diagnosis. When decalcification was necessary, rapid treatment with nitric acid though not entirely satisfactory was the best procedure.

[ED. NOTE—Jaffe's paper is of considerable value to orthopedic surgeons in helping to solve the troublesome technical problems that are always encountered when persons unfamiliar with bone sections are attempting to prepare them for histologic study. It is to be hoped that Morrell's new microtome knife will afford the means of avoiding cellular damage caused by decalcification, in which case it will represent a real step in progress.]

*Muscular Atrophy Following the Use of Apparatus*—Basing his conclusions on the results of examination of children with congenital dislocations of the hip who had had their luxations reduced three years previously, Gaugele<sup>41</sup> pointed out that the criticism of the use of apparatus because it caused muscular atrophy was not substantiated by fact. Children who had been cured of congenital dislocations showed normal muscular development in spite of the fact that they had worn plaster splints and other apparatus for many months. On the other hand, children with untreated dislocations showed muscular atrophy of varying degrees. His experience in the treatment in scoliosis had convinced him that the wearing of supports prevented the severe progressive atrophy that was otherwise found in this condition. He had never seen evidence of damage to the internal organs from corsets or braces, on the contrary, their use often resulted in improved function.

*Therapeutic Pools*—Lowman<sup>42</sup> expressed his belief that there was as much possibility for variation in exercises in an underwater gymnasium as in a regular gymnasium, with the added advantage that in the water the patient could be allowed to move in all planes whereas in the gymnasium, with the subject in the lying position, movements were

40 Jaffe, H. L. Methods of Histologic Study of Normal and Diseased Bone, Arch. Path. 8:817 (Nov.) 1929.

41 Gaugele, K. Ztschr. f. orthop. Chir. 51:74, 1929.

42 Lowman, C. L. Physical Equipment of Therapeutic Pools, J. A. M. A. 94:845 (March 22) 1930.

restricted to certain planes. The successful use, however, of various types of apparatus depended on the resourcefulness of the technician and her knowledge of kinesiography, especially of pathologic or abnormal kinesiography as it existed in paralytic patients of those in whom joint plaster surgery or tendon transplantation has been done. The surgeon's understanding of how and when to prescribe the different types of work is also essential for the successful treatment in any case.

*Operations on the Bones, Joints and Tendons, Anesthesia*—In an interesting and instructive article Koster and Kasman<sup>43</sup> discussed spinal anesthesia in the light of their experience with complete body anesthesia in 750 operative cases. They considered it perhaps the safest method of anesthesia and advocated its use not only in operations on the abdomen and lower extremities but also in operations on the chest, neck, head and upper extremities. They had no fear of respiratory embarrassment, and they had demonstrated in frogs and cats that application of the anesthetic directly to the medulla had no effect on respiration. They had never seen any adverse effect on the respiratory apparatus of man when anesthesia of the head and neck was obtained. They considered that the specific gravity of the injected solution had no effect in controlling the extent of diffusion of the drug. They insisted, however, that the degree of anesthesia depended directly on the amount of spinal fluid withdrawn before injection of the anesthetic, because the greater the amount of cerebrospinal fluid withdrawn, the greater would be the diffusion and therefore the higher the level of anesthesia. Decreases in blood pressure did not alarm them and they belittled the value of vaso motor stimulants. There were rarely serious complications from the use of spinal anesthesia, the chief ones being headache, diplopia, temporary paresthesia and urinary retention.

The greatest precaution taken by the authors was in the estimation of the proper dose of the drug. The details of this estimate were given, and the amount injected varied in proportion to the size and the age of the patient.

Francillon<sup>44</sup> recommended the use of local anesthesia in orthopedic operations. He expressed his belief that it possessed many advantages over general anesthesia. He had found the active muscular help of the patient of great importance in the transplantation of tendons, likewise in certain operations on the foot. He considered local anesthesia less dangerous than general anesthesia. In operations on the spine which necessitated the prone position of the patient, local anesthesia was especially advantageous as the difficulties and dangers in the use of general anesthesia in this position were much increased.

43 Koster, H., and Kasman, L. P. *Surg Gynec Obst* 49 618, 1929

44 Francillon, M. R. *Ztschr f orthop Chir* 53 60, 1930

*Arthrodesis of the Shoulder*—A technic for arthrodesis of the shoulder with the aid of osteoperiosteal grafts was described by Key<sup>45</sup>. He had used it for tuberculosis and paralysis of the deltoid. He exposed the shoulder through the saber-cut incision, dividing the acromioclavicular joint and retracting the tip of the acromion with the attached deltoid outward. As complete synovectomy as possible was performed. The glenoid and the head of the humerus were denuded of cartilage, as was the under surface of the tip of the acromion. Two inch (5 cm) osteoperiosteal grafts, which had previously been removed from the tibial surface, were then inserted subperiosteally between the glenoid and the head of the humerus. The arm was placed in 90 degrees of abduction and in about 25 degrees of anterior flexion. In tuberculous joints a nail was driven in through a stab incision, 3 inches (7.5 cm) below the head of the humerus, directly through the head into the glenoid. A plaster casing made the day before operation was then applied, the arm being held in the desired position.

*Stabilization of the Thumb*—Fitch<sup>46</sup> reported a method of arthrodesis of the first carpometacarpal articulation for paralysis of the opponens pollicis. The proximal end of the first metacarpal bone was first dislocated posteriorly. This produced a more advantageous functional position than when arthrodesis of the first metacarpal bone was made in normal relation to the greater multangular bone (trapezium).

*Combined Intra-Articular and Extra-Articular Fusion of the Tuberculous Hip*—Eikenbary and Le Cocq<sup>47</sup> devised a special technic for arthrodesis of the hip by a combined intra-articular and extra-articular method. A massive slab graft obtained from the ilium was fixed below in a split in the trochanter, above, it was in contact with the ilium, being anchored in place by a wire passed through the ilium from within the pelvis. They reported twenty-one cases in which the method had been employed with complete ankylosis of the hip and arrest of the disease in from six to twelve months postoperatively. They felt that extra-articular fusion alone was inadequate, as much tuberculous material was left in the joint which rendered the cure difficult. They did not consider draining sinuses a contraindication to operation.

[ED. NOTE—Eikenbary and Le Cocq's method of fusion seems sound and the results in a small number of cases are impressive.]

Galland<sup>48</sup> advocated the bifurcation operation of Lorenz in selected cases of traumatic, pathologic or congenital dislocations of the hip, in nonunited fractures of the neck of the femur and in inflammatory

45 Key, J. A. *Surg. Gynec. Obst.* 50:468, 1930.

46 Fitch, R. R. *J. Bone & Joint Surg.* 12:190, 1930.

47 Eikenbary, C. F., and Le Cocq, J. F. *Northwest Med.* 29:23, 1930.

48 Galland, W. I. *Surg. Gynec. Obst.* 50:90, 1930.



processes involving the hip joint, such as arthritis deformans, tuberculosis or Charcot's disease. The advantages of the operation, according to Galland, were. It relieved pain, a good functional and cosmetic result could usually be obtained, the operation was relatively simple (although it had to be performed with the utmost care) and the period of recumbency after operation was short. The dangers were injury to the femoral vessels by the distal fragment and nonunion. The author reported results in ten patients on whom the operation had been performed.

Reviewing the results of 103 operations on the hip joint that he had performed in the last twenty years, Ashhurst<sup>49</sup> stated that in his opinion the indications for typical arthroplasty had almost disappeared in the better development of the reconstruction operations of Whitman and Gill. He considered capsulorrhaphy a useful operation in paralytic dislocations of the hip. He had found reconstruction operations superior to bone pegging in fractures of the neck of the femur. Excision of the upper portion of the femur was indicated only as a life-saving measure, and in this case the author preferred Lambotte's incision. He found that the Smith-Petersen incision gave the best exposure for open reduction of the hip. Reconstruction operations had the widest field of usefulness in hip disabilities resulting from tuberculosis, pathologic dislocations, nonunion and chronic arthritis.

[ED. NOTE—Many orthopedic surgeons will question Ashhurst's statement as to the value of the reconstruction operation in tuberculosis of the hip.]

*Osteochondritis Dissecans of the Ankle Joint*—Laewen<sup>50</sup> discussed osteochondritis of the ankle joint which he had encountered in four patients and operated on with good result. He considered that spontaneous cure might result either by actual restoration of the affected area or by complete disintegration of the necrotic piece of bone, but he thought that this was a rare occurrence.

*Tarsal Autotransplants*—Curcio<sup>51</sup> reported two tarsal autotransplants for the correction of severe deformities of the feet. He performed a transverse section and in one instance removed the cuboid with a skin flap and inserted the bone and skin flap on the inner side of the foot in the space that was caused by correction of the deformity. In another instance the transplant consisted of the scaphoid and overlying skin, he inserted this in the wedge-shaped opening on the outer side of the foot made by correcting a valgus deformity.

49 Ashhurst, A. P. C. *Operative Surgery of Hip Joint*, Arch. Surg. 20: 57 (Jan.) 1930.

50 Laewen, A. *Zentralbl. f. Chir.* 56: 2498, 1929.

51 Curcio, A. *Chir. d. org. di movimento* 14: 216, 1929.

[ED NOTE—Curcio's autotransplantation of a portion of the tarsus with the overlying skin is of little practical value but it is interesting as it adds to the orthopedic surgeon's armamentarium for dealing with unusual conditions]

*Hallux Valgus*—Brandes<sup>52</sup> related his experiences with the operation for resection of the proximal two thirds of the first phalanx of the great toe for hallux valgus. He had performed this operation in more than 100 patients with good anatomic and functional results. He did not disturb any of the other structures of the foot except to remove with a chisel the prominent portion of the inner side of the head of the first metatarsal bone. After closure of the wound, he placed the toe in slight plantar flexion to avoid infolding and necrosis of the skin. He applied a plaster of paris foot plate, fixing the foot in slight plantar flexion and adduction. At the end of two weeks, he permitted the patient to walk with a metatarsal strapping.

[ED NOTE—The operation described by Brandes is the same as that devised by Keller in America many years ago except that it removes more of the proximal phalanx of the great toe than we would consider necessary]

#### FRACTURES

*Occupational Therapy*—Miss Taylor<sup>53</sup> discussed the value of occupational therapy in industrial injuries, and stated her opinion that a combination of physical therapy and occupational therapy achieved the greatest success in the treatment for industrial injuries as measured by the shortening of the period of disability. The occupational therapy ought to be carefully planned for the type of injury and the psychologic point of view of the patient. The injuries most commonly requiring treatment were those of the hand. With most of the conditions the greatest gain could be obtained if the treatment was begun in the first three weeks. The commonest disability was flexion, and the greatest danger was that of over-fatigue from too continuous contraction of muscles.

*Fracture of the Capitellum of the Humerus*—In a report of three cases of fracture of the capitellum of the humerus, Ciaccia<sup>54</sup> emphasized the fact that this was a rare injury, only a few cases having been described in the literature. He had recognized two types—one in which there was displacement of the cartilage of the capitellum with a small section of the bone and one in which the fragment consisted of the capitellum and the outer lip of the trochlea. The treatment suggested was removal of the fragment which according to the author, resulted in

52 Brandes, M. Zentralbl. f. Chir. 56 2434, 1920

53 Taylor, M. Occup. Therapy 8 335 1929

54 Ciaccia, S. Chir. d. org. di movimento 14 181, 1929

complete or nearly complete restoration of function. Lateral as well as anteroposterior roentgenograms were essential for studying the condition.

*Compression Fractures of the Vertebrae*—Rogers<sup>55</sup> devised a frame for the correction of compression fracture of the vertebrae. It was essentially a Bradford frame, with flexible side pieces and a cross-bar capable of being elevated, which could be moved to any point under the frame. The patient lay in the dorsal decubitus on the tight canvas cover and the spine was gradually hyperextended by cranking up the cross-piece, the correction of the fracture was gained by means of the action of gravity on the spine above and below. Maximum correction was usually obtained in about ten days. The patient could then be placed on a hyperextended Bradford frame where the correction was maintained for an additional eight weeks. This was followed by the use of an ambulatory plaster jacket for several months.

Dunlop and Parker<sup>56</sup> reported that they had corrected the deformity of vertebral compression fractures by a method of forcible hyperextension and that by this means they had obtained restoration of the normal form of the vertebrae in twenty-one patients. The patient was anesthetized and placed in the supine position, and folded sheets were passed across under the injured segment. Holding the ends of the sheets, the operator and his assistant suddenly made these taut, tossing the patient upward, at the same time, traction and countertraction were made by two persons pulling on the opposite ends of the patient's body. Following the reduction, care was taken to keep the body in a position of hyperextension, and a plaster jacket was applied with the aid of Goldthwait's frame.

Hempel<sup>57</sup> believed that he had found a way to avoid the dangers of forcible methods and at the same time to secure complete anatomic and functional restoration of the spinal column. He placed the patient on a hard, smooth mattress, at first in the supine position, but after a few days, in the prone position so that he could prop himself on his elbow. Boards were placed under the mattress to prevent sagging. As soon as the pain caused by the fracture had diminished, the muscles of the back were massaged and after seven weeks the patient was permitted to crawl on all fours as a regular exercise. Having become proficient in this exercise, the patient was next permitted to stand and finally to sit.

[ED. NOTE—Within the last two years great advances have been made in the treatment for compression fractures of the spine. Reduc-

55 Rogers, W. A. *Surg. Gynec. Obst.* **50**: 101, 1930.

56 Dunlop, J., and Parker, C. H., *Correction of Compressed Fracture of the Vertebrae*, *J. A. M. A.* **94**: 89 (Jan. 11) 1930.

57 Hempel, C. *Deutsche Ztschr. f. Chir.* **223**: 79, 1930.

tion of deformity is henceforth to be sought in this instance just as in other fractures. Several methods of reduction have been devised, beginning with the method of forcible reduction of Davis. Without personal experience of either the methods of Davis or those of Dunham and Parker, we would prefer the former to the latter as attended by less risk. Rogers' method of gradual hyperextension is the safest of all these methods as it entirely avoids the use of force. We have watched this method in use and can speak for its effectiveness. Whether the reduction accomplished by it is as complete as that obtained by the forcible methods will be decided in time. Hempel's method does not appear to us to be effective, nor is it logical to trust only to the muscles instead of to apparatus for protection. There is reason to hope that by the correction of deformity and by thorough and prolonged splinting to prevent recurrence of the deformity, the serious disabling effects of fractures of the vertebrae may be greatly diminished.]

*Fractures of the Transverse Processes*—A study was made by Quaintance<sup>58</sup> of nonunion and disability in thirty-three patients with fractures of the transverse processes. In 85 per cent of the patients the fracture involved the second, third and fourth transverse processes. More than 50 per cent of the fractures were produced with the body in a position of acute flexion. Of a total of seventy-five fractures nonunion occurred in 14, or in 18 per cent. In every instance of nonunion there had been wide separation of the fragments. None of the patients was permanently disabled, even with associated injuries of the pelvic bones, vertebrae and ribs which occurred in nine patients. The longest period of disability was seven months. Resection of the fractured transverse process was not necessary in any instance.

*Fractures of the Pelvis*—Noland and Conwell<sup>59</sup> reported the treatment and results in a group of 125 patients with fractures of the pelvis. Only 39 of the patients had a single fracture of the pelvis. The fractures were divided into 3 groups: (1) single fractures in which the continuity of the weight-bearing ring was preserved, (2) multiple fractures in which it was necessary to relieve the bones of weight until the fracture was consolidated, and (3) the double vertical fracture (Malgaigne's fracture) usually accompanied by extensive dislocation of the whole pelvis. The anterior ring fractures and marginal fractures gave the best results. Fractures of the acetabulum yielded fair results, but in the fractures involving the posterior ring about the sacro-iliac joint the poorest results were obtained, disability ranging from 25 per

<sup>58</sup> Quaintance, P. A. Fracture of the Lumbar Processes of the Transverse Vertebrae. Arch Surg 10 968 (Dec.) 1930.

<sup>59</sup> Noland, L. and Conwell, H. E. Acute Fractures of the Pelvis, J. A. M. A 94 174 (Jan 18) 1930.

cent to almost permanent total disability. When discharged, only about 60 per cent of the patients had what was called good anatomic position, but the authors were sure from their observations that excellent functional results were frequently obtained in cases in which good anatomic position was by no means secured. Open reduction for correction of displacement of bony fragments was done in only two instances, and then only to relieve pressure of the displaced fragments on the rectum and bladder. The authors were of the opinion that what appeared to be a poor position of the fragments was by no means a constant cause of persistent pain and disability. The average number of days lost from work in both industrial and civilian cases was 175. It was noticeable that the majority of civilian patients returned to their work much earlier than did the industrial patients.

*Fractures of the Neck of the Femur*—Hey-Groves<sup>60</sup> reviewed the results in 24 of his own cases and in 116 other cases of fractures of the neck of the femur reported from three large English hospitals. In the latter group he found nonunion in 23 per cent and poor or bad results in 53.3 per cent of cases. He concluded that patients with basal fractures might be treated successfully either by traction or by the Whitman abduction method, traction probably being better as it permitted earlier motion of the hip. In true intrascapular fractures treatment involved a choice between the Whitman abduction method and the pegging operation. For young and vigorous persons, the author preferred pegging, i. e., the insertion of a beef bone peg in a hole bored through the proximal fragment into the trochanter. In other patients in whom the Whitman method was used, pegging could be resorted to if roentgenograms showed nonunion at the end of three months. When operation revealed that the proximal fragment had lost its cartilage and that the bone was soft and friable, it was much better to remove the head and perform a reconstruction operation.

Albee<sup>61</sup> wrote enthusiastically of the results of treatment for non-united fractures of the neck of the femur by the operative insertion of autogenous bone pegs. Thirty-six patients had been treated in this manner. For the treatment in fresh fractures of the neck of the femur, he did not believe that the Whitman procedure could be improved on, in cases of delayed union or nonunion, however, he preferred the bone peg operation or reconstruction procedure. In the bone peg operation he used two incisions. The peg was made from a tibial graft and driven in through a drill hole made from a point just below the greater trochanter through the neck into the femoral head. He stated that over 90 per cent of the patients so treated had obtained union. He was

60 Hey-Groves, E. W. *J. Bone & Joint Surg.* **12** 1, 1930.

61 Albee, F. H. *Surg. Gynec. Obst.* **49** 810, 1929.

opposed to the use of nails or other material for the fixation of the fragments. The choice between the bone peg operation and the reconstruction operation depended on the cooperation of the patient, the duration of the fracture and the condition of the fragments at the time of operation. Often the decision could not be made until operation when the fragments were actually exposed.

*Fractures of the Bones of the Foot Other Than the Os Calcis*—In considering fractures of the bones of the foot other than the os calcis Brown and Brown<sup>62</sup> made the following grouping in relation to their importance to function: (1) fractures of the astragalus, (2) fractures of the inner tarsals which, with the first, second and third metatarsals constituted the longitudinal arch, (3) fractures of the fourth metatarsal, (4) fractures of the fifth metatarsal and (5) fractures of the phalanges and sesamoids.

In a group of forty-six fractures of bones of the foot excluding the os calcis there were twenty-eight single and eighteen multiple fractures. The incidence was about the same for fractures of the metatarsals except for the fourth metatarsal which was smallest. There was one fracture of the astragalus, one of the cuneiform and two of the sesamoids. The average loss of time for a fracture of the metatarsal was forty-six days and for a fracture of the phalanx thirty-three days.

#### DISLOCATIONS

*Dislocation of the Cervical Vertebrae*—From an experience with seventeen bilateral cervical dislocations and thirteen unilateral dislocations Langworthy<sup>63</sup> believed that reduction by the method of Walton should be tried in all cases provided that the roentgenograms showed no evidence of fracture or disease. To be sure of preventing redislocation, which may occur as late as ten days after reduction, a plaster casing should be applied.

All the patients with unilateral dislocations showed complete recovery from symptoms. Five of the patients with bilateral dislocations died, and five of eight patients showed serious injury to the spinal cord.

*Old Dislocations of the Shoulder*—Key<sup>64</sup> presented the histories of two cases of old dislocation of the shoulder, both of the subcoracoid type. He stated as a general rule that dislocations of eight weeks' duration or less could be reduced by manipulation while dislocations of twelve weeks' duration or more required open operation. In manipula-

62 Brown W L and Brown C P. Fractures of the Bones of the Foot Other Than the Os Calcis. J A M A 94 461 (Feb 15) 1930.

63 Langworthy M. Dislocation of Cervical Vertebrae, J A M A 94 86 (Jan 11) 1930.

64 Key I A. Missouri State M A J 27 129, 1930.

itself excised. If there is any doubt as to the usefulness of the artery either as a main blood carrier or as the seat of collateral vessels, this procedure should be condemned.

The effect of the removal of the sympathetic supply to veins is an open question. In weighing the results of the operation described, judgment must be reserved as to the possible influence here.

One must not expect the removal of the perivascular sympathetics by arteriectomy to have a more permanent effect than results from removal by stripping. At the most, the effect may last from four to six weeks. In case 4 of the present series the time limit of the effect was well demonstrated. If by the operation sufficient hyperemia of the collaterals can be obtained to carry an extremity over the critical period of acute ischemia, much may be accomplished. In an occasional case this may mean ultimate salvation of the limb. Arteriectomy in cases of complete arterial occlusion is probably preferable to perivascular sympathectomy, because the removal of the fibers is more certain, more complete and much less difficult.

A further development of the idea of encouraging collateral circulation by operation on the sympathetic must be mentioned. If favorable effect can be shown by perivascular sympathectomy, it is logical to suggest that the more positive, permanent and rational operation of sympathetic ganglionectomy may have a place. If, for instance, one could diminish by lumbar sympathetic ganglionectomy the incidence of gangrene following acute division of the popliteal artery, a real addition would be made to one's resources. Experimental work now being carried on in my laboratory is directed toward the clarifying of this point.

There is a possibility that the ideas here expressed may help to clear up certain confused issues relating to this subject. If in every published report of ligation of a major vessel a detailed description of the operation were included, the confusion might in part disappear. It becomes essential to know in every such instance whether the ligation is accompanied by division or by excision of the artery, or by neither. Let me make a plea, parenthetically, for such information.

In conclusion I must emphasize that I have presented no indisputable evidence that arterial excision improves collateral circulation by sympathectomy. I have presented suggestive evidence with the reasoning based thereon.

I urge only that in any instance of arterial occlusion in which excision is possible and apparently harmless it be done with the intent to observe the results. Thereby the knowledge of these obscure phenomena may be increased. I suggest that thereby good results also may come to the individual patient.

# SPLENECTOMY IN GAUCHER'S DISEASE \*

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The literature on Gaucher's disease, by reason of its comparative paucity, has been kept well abreast of the time. It seems unnecessary to record a review of it.

At the Mayo Clinic, in 530 cases in which splenectomy was performed during the period of seventeen years, 1913 to 1929, inclusive, Gaucher's disease was encountered four times. In this article I shall not enter into a discussion of the theories advanced as to the etiology and pathology of the disease. Records of cases are given in detail as far as possible. I have been particularly interested in the value of splenectomy in this group, and there would seem to be a well grounded impression that in patients who have reached maturity removal of the spleen has a definitely beneficial effect.

## REPORT OF CASES

CASE 1.—A woman, aged 30, came for examination on Jan. 26, 1920. She had married at the age of 17, and was the mother of eight children, all living and well. Her menses were regular, and she had had no miscarriages. Her chief complaint was a floating left kidney, which had been discovered seven years previously. For two years she had noted ready exhaustion and some dyspnea on exertion. There had been no edema of the extremities, no abdominal pain or discomfort and no urinary symptoms.

General examination disclosed a large mass filling the left upper abdominal quadrant. It had a sharp median edge suggestive of a greatly enlarged spleen. The thorax was negative to general and roentgenologic examinations. Nothing significant was noted in roentgenograms of the urinary tract. Results of urinalysis and of the Wassermann reaction of the blood were negative. Renal function was satisfactory. Examination of the blood was made on January 27.

The concentration of hemoglobin (Dare) was 80 per cent, erythrocytes numbered 4,760,000 and leukocytes 4,600 in each cubic millimeter of blood. Results of a differential count of 200 leukocytes were as follows: polymorphonuclear neutrophils, 78.5 per cent, lymphocytes, 20.5 per cent, and eosinophils, 1 per cent. The bleeding time was two and a half minutes and the coagulation time was four minutes. Fragility of erythrocytes was normal. A pyelogram of the left kidney disclosed some downward displacement and rotation of the renal pelvis with acute angulation of the ureter at the ureteropelvic juncture. A tentative diagnosis of a large cyst in the upper pole of the left kidney or of an extrarenal tumor was made.

Exploration through an anterior abdominal incision was advised. Operation on February 25 revealed a splenic tumor surrounded by dense adhesions. It was

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\* Submitted for publication, Feb. 27, 1930.

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removed with some difficulty and with slight loss of blood. The left kidney was found to be displaced below the spleen, was movable, but not sufficiently diseased to warrant removal. The gallbladder, stomach and appendix were normal. The weight of the spleen was 1,450 Gm. The pathologic diagnosis was Gaucher's disease (fig 1).

The patient made an uneventful convalescence and was dismissed from the hospital on the twelfth postoperative day. Examination of the blood on March 16 disclosed a concentration of hemoglobin (Dare) of 61 per cent. Erythrocytes numbered 3,620,000 and leukocytes 7,800 in each cubic millimeter of blood. A differential count of 200 leukocytes gave the following result: polymorphonuclear neutrophils, 59 per cent, lymphocytes, 37 per cent, eosinophils, 1 per cent, and basophils, 3 per cent.

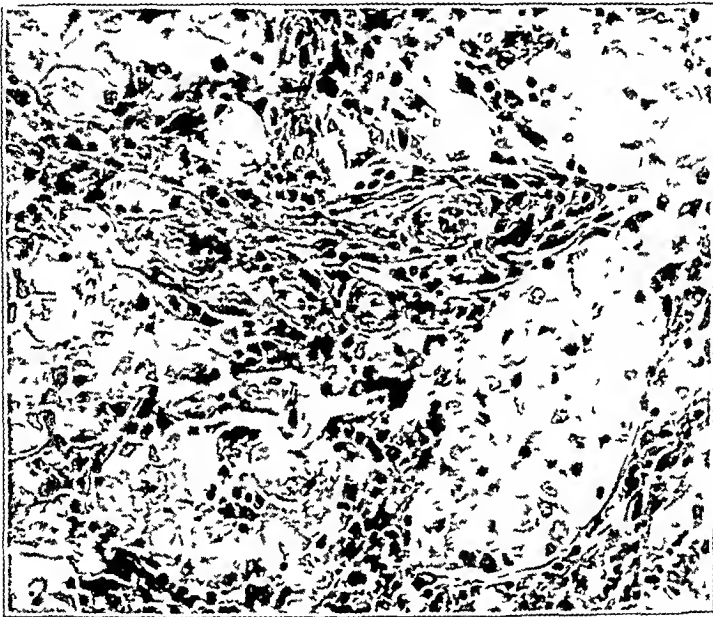


Fig 1 (case 1) —Characteristic Gaucher's cells in spleen,  $\times 250$

The patient's family physician, under date of Dec 18, 1929, wrote: "She has been in the best of health since her operation. Has gained greatly in flesh, has been doing most of the work in a large family, and seemingly is good for a long life. I have confined her three times since her operation and she has done finely. These three children are healthy and strong, the last one being three months of age."

**CASE 2**—An unmarried woman, aged 36, came for examination on account of "female" trouble on May 15, 1923. She had two brothers and five sisters, all living and well. She had had pneumonia in infancy. Menstruation had begun when she was 13 years of age and had been regular until two years before she came to the clinic, when her periods had stopped abruptly. About the same time during an attack of dengue her physician had discovered that she had an abdominal tumor which had been thought to be an ovarian cyst or uterine fibroma. She stated that there had been some enlargement of the liver as far back as she could remember. Jaundice had never been noticed except during the attack of dengue. No history of abdominal pain or of loss of weight was elicited.

General examination revealed irregular enlargement of the abdomen. The sharp edge of a smooth liver could be felt reaching 17 cm below the right costal margin, in the paramammary line. At this level, and occupying the central zone of the lower half of the abdomen was a mass about 15 cm in diameter with an upper edge suggesting that of a greatly enlarged spleen. This mass could be palpated by vaginal examination in the anterior and left lateral culdesacs.

Nothing significant was found in the thorax on either general or roentgenologic examination. Roentgenograms of the urinary tract gave negative results. In the urine heavy traces of albumin, a few hyaline casts and erythrocytes and pus cells in small numbers were found. Renal function and blood urea were within normal limits. The Wassermann reaction of the blood was negative. There were no pathologic changes in the eye grounds. The blood picture was determined on

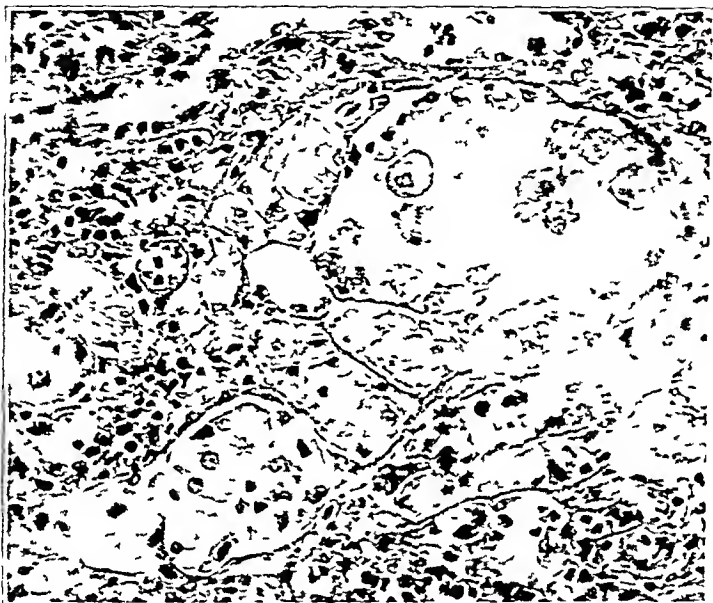


Fig 2 (case 2) —Characteristic Gaucher's cells in spleen  $\times 250$

May 16. The concentration of hemoglobin was 80 per cent, the number of erythrocytes was 4,460,000, leukocytes 4,800 and platelets 112,000 in each cubic millimeter of blood. A differential count of 200 leukocytes disclosed the following: lymphocytes, 25.5 per cent; large mononuclears, 2 per cent; transitionals, 2 per cent; neutrophils, 69.5 per cent; eosinophils, 0.5 per cent; and basophils, 0.5 per cent. The coagulation time was eight minutes and the bleeding time one and a half minutes. A diagnosis was made of a lower abdominal or pelvic tumor associated with a greatly enlarged liver and exploration was advised.

Operation was done on May 22, 1923. The lower abdominal tumor proved to be splenic; it lay in the pelvis by reason of a long pedicle. Removal was accomplished without difficulty or hemorrhage. The liver was enlarged, hard and friable. The uterus was atrophic. The pathologic diagnosis was Gaucher's disease. The spleen weighed 2,800 Gm (fig 2).

The patient made an uneventful convalescence and was dismissed from the hospital on the sixteenth day following operation. Under date of August 15, 1925, she wrote: "My color is good and my general health has been excellent. Have been gaining weight rapidly. My liver is still very large. Have not had to consult a physician since my operation more than two years ago. The last report

concerning the patient was from a friend, who stated that she had died very suddenly on May 24, 1929. The cause of death was given as cerebral hemorrhage.

CASE 3—A woman, aged 26, of Jewish extraction,<sup>7</sup> who had no brothers or sisters, presented herself for examination on Sept 7, 1927. She had married at 19 years of age, but never had been pregnant. She had scarlet fever in childhood. Menstruation had begun at the age of 13 years and had been somewhat irregular but without excessive flow. When she was 7 years of age her family physician had discovered, in a routine examination, that her spleen was enlarged. In spite of fairly marked anemia she had taken part in the ordinary pleasures and outdoor sports of youth. She always had been more easily exhausted than her companions. At the age of 9 years, she had been seen by a leading internist, who had made a diagnosis of Banti's disease, and he had advised splenectomy. Owing to the high risk given, surgical treatment had not been accepted, but several treatments with roentgen rays applied over the enlarged spleen had been tried. One year before she came to the clinic she had undergone tonsillectomy, and the operation had been followed by local hemorrhages. A month before she was seen at the clinic, she had a tooth extracted, and profuse gingival bleeding had persisted for two days. For the year prior to her registration at the clinic the patient had noticed rapid enlargement of the already large spleen. Sufficient food could not be taken at a meal without much distress afterward.

On examination, the patient was found to be somewhat anemic and in a fair state of nutrition. Pingueculae on the nasal side of each cornea were noted. The thorax was normal except for diminished breath sounds. The abdomen was greatly enlarged by a splenic mass which extended into the pelvis. The liver was moderately enlarged. No superficial lymph nodes of significant size were found.

Traces of albumin were found in the urine. The Wassermann reaction of the blood was negative. A roentgenogram of the thorax disclosed localized evidence of bronchiectasis in the lower lobe of the right lung. Complete examination of the blood was made on September 7. The concentration of hemoglobin was 51 per cent. Erythrocytes numbered 3,570,000, leukocytes 5,200, and platelets 86,000 in each cubic millimeter of blood. A differential count of 200 leukocytes disclosed the following: lymphocytes, 20 per cent, large mononuclears, 2 per cent, transitionals, 0.5 per cent, neutrophils, 76.5 per cent, eosinophils, 1 per cent, and reticulocytes, 3.5 per cent. The coagulation time was eleven and a half minutes (Lee method), and the bleeding time five minutes. Prothrombin time was prolonged in all tubes. Fragility of erythrocytes was normal. A dye retention test of hepatic function gave negative results. The concentration of serum bilirubin was 2.4 mg per hundred cubic centimeters. The van den Bergh reaction was indirect. Gaucher's disease was the most probable diagnosis. A further trial of radiotherapy seemed more advisable than surgical treatment.

Following the treatment, the patient returned to the clinic, on October 17, for reconsideration of her condition. She felt much better and thought there had been some decrease in the splenomegaly. On this date the concentration of hemoglobin (Dare) was 49 per cent. Erythrocytes numbered 2,850,000 and leukocytes 2,300. The bleeding time was twenty-two and a half minutes. The high risk of splenectomy did not seem to be warranted, and radiotherapy was again advised. At reexamination on November 28, the patient still maintained that her spleen had become smaller. The liver was not so large as in September. On November

<sup>7</sup> In the cases in which the patients were of Hebrew extraction the fact is noted because formerly it was believed that this disease was peculiar to Jews. This belief has not been sustained.

28, the concentration of hemoglobin (Dare) was 46 per cent. Erythrocytes numbered 3,303,000, leukocytes 2,900 and platelets 76,000 in each cubic millimeter of blood. Coagulation time was eleven minutes (Lee), and calcium time, fourteen minutes, prothrombin time was prolonged in all tubes, and bleeding time was five and a half minutes. Retractility of the blood clot was marked in one hour and complete in three hours. The status of the patient made a decision as to future treatment somewhat of a dilemma, but operation finally was decided on.

Operation was performed on December 1. A huge spleen, projecting down into the pelvis, was found and was removed without great difficulty. The liver was large and there were tiny, shotlike nodules over it. A small piece of the right lobe was excised for examination. The gallbladder was distended, but no stones were felt in it. The spleen weighed 3,240 Gm., the spleen and a specimen of liver showed changes characteristic of Gaucher's disease (fig. 3).

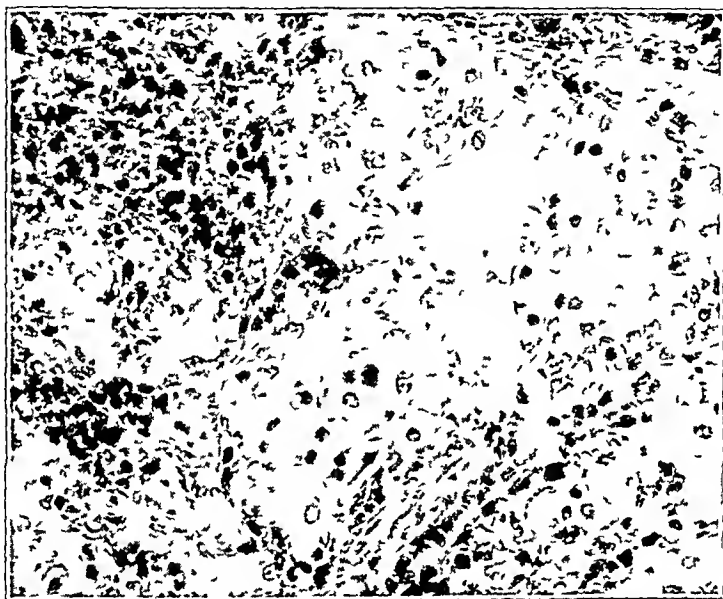


Fig. 3 (case 3) —Characteristic Gaucher's cells in spleen,  $\times 250$

Convalescence was uneventful and the patient was dismissed from the hospital on the fourteenth postoperative day. During her stay in the hospital repeated tests of bleeding time were made and each showed it to be prolonged, ranging from twenty to fifteen minutes. At the same time, her blood platelets were rapidly increasing, from 264,000 on the twelfth day following operation to 480,000 on the fifteenth day. There were no hemorrhages at any time following splenectomy. The patient remained well and was not seen again until July 6, 1929. During the previous winter she had had pains in the right thigh and leg that had responded to treatment by heat and salicylates. She had gained from 10 to 12 pounds (4.5 to 5.4 Kg.) in weight. Menstruation had ceased until January, 1929, when she had had a normal flow for five days, followed by amenorrhea to the time of this last visit to the clinic.

General examination at this time did not reveal palpable enlargement of the liver, there was no adenopathy and nothing significant in the pelvis. On July 6, 1929, the concentration of hemoglobin (Dare) was 65 per cent, erythrocytes numbered 4,190,000, leukocytes 16,000 and platelets 168,000 in each cubic millimeter of blood. The differential leukocyte count was normal.

It was during this visit that changes in the long bones associated with Gaucher's disease were discovered in the roentgenologic examination. Complete roentgenologic examination of the skeleton in July, 1929, revealed the thorax, spinal column, pelvis and skull to be negative for changes characteristic of Gaucher's disease. There was enlargement of the medulla and thinning of the cortex of the humerus (fig 4), radius and the upper end of the femur (fig 5) on both sides.

The lesions demonstrable were of uniform type. The most marked change, general decrease in density, might be compared with senile osteoporosis. The

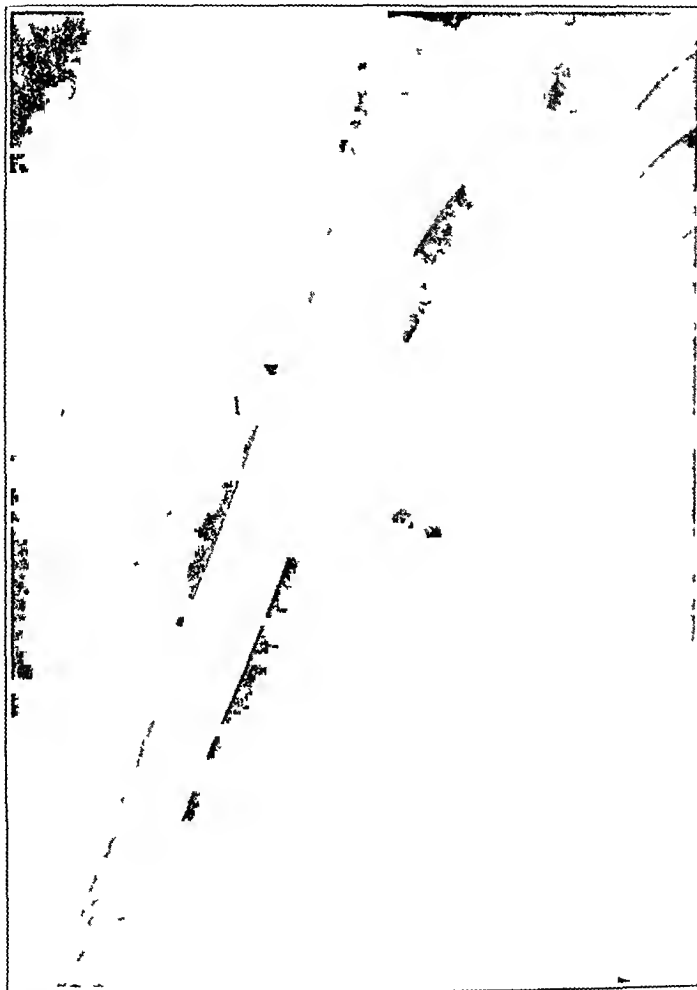


Fig 4 (case 3) —Right humerus, enlargement of the medulla and thinning of the cortex are evident

cortex, although markedly thinned, did not contain any areas of destruction. Trabeculation of the medulla was not as fine as it normally is and the trabeculae appeared to have been pushed apart by some process between them rather than by actual destruction by malignant cells. These changes were most marked in the shafts of the bones. The lower ends of the femurs were somewhat widened.

Considered from the standpoint of differential diagnosis, the picture was rather typical of the bony changes in Gaucher's disease. There was no definite, well circumscribed region of destruction of bone suggesting metastasis or multiple myeloma.

This patient's general condition has remained satisfactory over a period of more than two years following splenectomy. Her domestic and social duties are carried on with ease as compared with the preceding two years of abdominal distress, progressive fatigability and advancing anemia. With the hemorrhagic tendency which was clearly manifest, the surgical risk of splenectomy was high, but that operation as a mode of treatment was well chosen would seem to be established by the period of good health the patient has enjoyed since.

CASE 4—A Jewish woman, aged 33, married and the mother of one child who was in good health, came to the clinic on Oct 22, 1928, seeking relief for recurring infections in the nares, associated with headaches. She had typhoid fever when she was 5 years old. Menstrual irregularities had not occurred. There had been occasional bleeding from hemorrhoids.



Fig 5 (case 3) —Widening of lower ends of femurs

General examination revealed enlargement of the spleen, the organ extended to the median line of the abdomen and to the level of the umbilicus. Enlargement of the liver could not be detected. There were small corneal pingueculae. Bilateral vestibulitis was found on examination of the nose and throat. The tonsils were small and fibrous. A passed specimen of urine contained a large amount of albumin. The Wassermann reaction of the blood was negative. Roentgenologic study of the thorax and long bones gave negative results. A concentration of hemoglobin (Dare) was 65 per cent. Erythrocytes numbered 4,140,000 and leukocytes 12,100 in each cubic millimeter of blood. A differential count of 200 leukocytes disclosed the following: lymphocytes 13 per cent, large mononuclears 25 per cent, transitionals, 25 per cent, and neutrophils 82 per cent. A diagnosis of "possible Gaucher's splenomegaly" was made and splenectomy was advised.

Operation was postponed by the patient until June 5, 1929. At this time it was found that there had been some increase in the size of the spleen. There had been no new symptoms of note. A spleen weighing 1,000 Gm. and an accessory spleen of 125 Gm. were removed. The liver appeared normal. Stones could not be felt in the gallbladder. Pathologically, there were changes characteristic of Gaucher's disease in the spleen and in an accessory spleen (fig. 6).

Convalescence was uncomplicated. On the day following operation the leukocytes rose to 46,800, in a week they receded to 22,000. The number of blood platelets increased from 292,000, June 6, to 852,000 a week later. There were no appreciable changes in estimations of hemoglobin and erythrocytes. The patient was dismissed from the hospital on the fourteenth postoperative day. She was seen two months later in excellent condition. At that time, the concentration of hemoglobin was 70 per cent. Erythrocytes numbered 4,140,000 and leukocytes 13,000 in each cubic millimeter of blood. The differential count was normal. The urine contained only a slight trace of albumin.

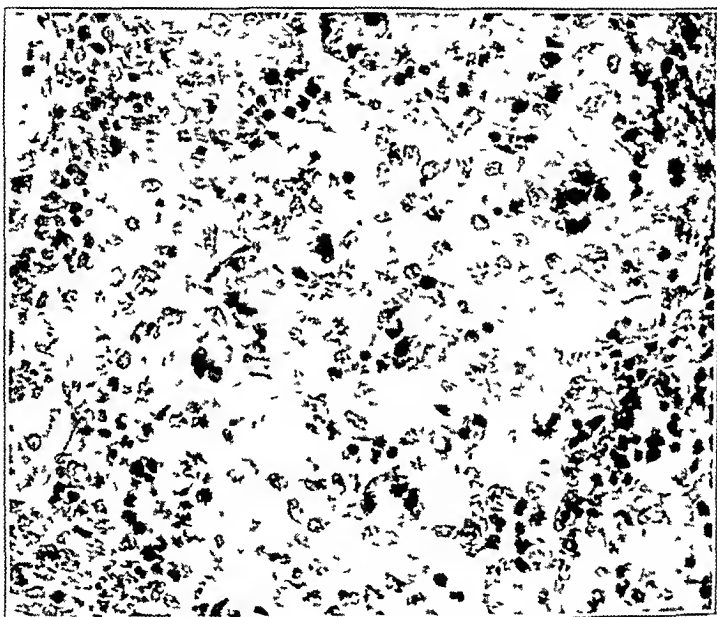


Fig. 6 (case 4) —Characteristic Gaucher's cells in spleen,  $\times 250$

#### COMMENT

Four cases of Gaucher's disease, in which splenectomy was performed are reported. All of the patients were women. The age at the time of operation ranged from 26 to 36 years. There was no history of familial tendency to the disease in any of the four patients. Two of the four patients are definitely known to belong to the Jewish race.

Gaucher's disease may not make any particular inroad into the general health of a patient. The unusual splenomegaly is the most frequent cause leading the patient to seek medical aid. Anemia was not present in cases 1, 2 or 4.

Three of the four patients have enjoyed periods of good health following splenectomy ranging from seven months (case 4) to almost

ten years (case 1) Only one patient (case 2) has died She lived for more than two years following splenectomy The cause of death was cerebral hemorrhage

Nothing significant has been discovered so far in the blood picture of Gaucher's disease to establish the diagnosis Removal of a lymph node, splenic puncture, or trephining of the bone-marrow would seem to be warrantable means to employ in determining whether a case of obscure splenomegaly belongs to the group of Gaucher's disease The roentgenographic changes in the bones may also be of great value in the final diagnosis These changes are well shown in the roentgenograms taken in case 3 Hemorrhagic diathesis may be an outstanding feature of the disease, as illustrated in case 3

Gaucher's disease in the female does not preclude the possibility of pregnancy, but that it may affect the menstrual life of the patient seems to be suggested In the second patient there was abrupt cessation of menstruation in the thirty-fourth year The third patient has had a long period of amenorrhea since splenectomy, but the possibility that this may have been in part due to previous radiotherapy needs to be considered

Splenectomy for Gaucher's disease although not to be regarded as curative, must be looked on as a means of affording great relief to the patient, and possibly of arresting indefinitely the course of this obscure malady



# OCCURRENCE OF A TOXIC PROTEOSE FRACTION IN MATERIAL FROM VARIOUS SOURCES ~

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A toxic proteose fraction has been isolated by Whipple and his co-workers<sup>1</sup> from the intestinal content obtained from patients with acute intestinal obstruction and from animals with obstruction experimentally produced. This observation has been confirmed by others, and the chemical nature of this fraction has been subjected to further investigation by Ingvaldsen and his co-workers<sup>2</sup>. Ellis<sup>3</sup> has been successful in isolating a toxic proteose fraction from the intestine of dogs dying from distemper, peritonitis and following operation on the adrenal gland and from animals dying from the administration of this material. The factors responsible for the production of this material and the rôle that it may play in various intoxications are unknown. It was thought that further information concerning its origin and significance might be obtained by investigating its occurrence in material from additional sources.

It is to be understood that the term, toxic proteose fraction, as used in this article refers to a certain fraction obtained by the methods of separation described by Whipple<sup>1</sup> and by Ellis<sup>3</sup> and does not imply that the toxic substances in this empyric fraction are necessarily proteoses in nature. We did not attempt to purify the fractions beyond the stages outlined by the foregoing investigators, because we wished to avoid loss and destruction of the material. Both methods of separation were found to be about equally efficient. For the identification of the fraction we have followed the symptoms, the changes in the blood and the gross pathologic processes induced in unanesthetized dogs by its intravenous administration.

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Submitted for publication, March 18, 1930

<sup>1</sup> From the Department of Physiology, State University of Iowa

1 Whipple, G H, Rodenbaugh, F H, and Kilgore, A R. Proteose Intoxication, *J Exper Med* **23** 123, 1916

2 Ingvaldsen, T, Whipple, A O, Bauman, L, and Smith, B C. The Role of Anhydremia and the Nature of the Toxin in Intestinal Obstruction, *J Exper Med* **39** 117, 1924

3 Ellis J W. Cause of Death in High Intestinal Obstruction, *Ann Surg* **75** 429 1922

## EXPERIMENTAL WORK

*Normal Intestine*—In order to evaluate properly our observations it was necessary to know the degree of toxicity of normal intestine. The literature concerning this question is conflicting. Davis and Stone,<sup>4</sup> Whipple and his co-workers,<sup>5</sup> Ellis<sup>3</sup> and other investigators have regarded it as being practically nontoxic. Other workers have found it to have a variable degree of toxicity. Our investigation is limited to a study of the occurrence of the toxic proteose fraction and is not concerned with toxins of any other nature that may be present. The dogs were killed with chloroform or ether. The entire small intestine was removed, slit open and the mucosa and adherent content scraped away. The proteose fraction was prepared from this material in the usual way. The animals were selected from the stock used for experimental purposes and had been without food for the previous twenty-four hours. Nothing abnormal was noted about the animals, or the condition of their intestines.

When the material was prepared from the small intestine of a single average-sized animal we invariably failed to obtain a fraction that would cause definite intoxication or death. However, when the fractions from four or more intestines were compounded and injected into a single animal, the effect was always severe intoxication or death. We can say from our experience that one intestine yielded approximately one fourth of a lethal dose of this fraction. The symptoms and pathologic changes were indistinguishable from those observed when the material was prepared from the content of an obstructed intestine. Fatal doses usually caused death in from six to eighteen hours. The symptoms and pathologic changes have been described in detail by others.<sup>1</sup> The animals might appear normal for a few minutes after injection and then show vomiting, salivation, prostration, retching, bloody diarrhea and coma. The blood showed a rise of nonprotein nitrogen, concentration of cells and sometimes a decrease of the chlorides. The necropsy showed splanchnic congestion and hemorrhages which were most prominent in the duodenum but which often extended throughout the entire intestine. Blood was present in the lumen of the intestine. Although our experiments were somewhat limited, we failed to find that autolysis of the fresh intestine with chloroform and toluene appreciably increased the yield of this material.

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4 Davis, D. M., and Stone, H. B. Studies on the Development of Toxicity in Intestinal Secretion. *J. Exper. Med.* **26**: 687, 1917.

5 Whipple, G. H., Stone, H. B., and Bernheim, B. M. A Study of a Toxic Substance Produced by the Mucosa of Closed Duodenal Loops. *J. Exper. Med.* **17**: 307, 1913.

*Obstructed Intestine*—We have been able to confirm the observations of previous investigators as to the occurrence of a toxic proteose fraction in the small intestine of dogs dying from obstruction experimentally produced or from an injection of the proteose fraction. In addition, we have been able to obtain it from the content of closed colon loops which were removed after a duration of two weeks. We were able to prepare a lethal dose from the small intestine of a man dying from Hodgkin's disease. The small intestine from a child, aged 16 months dying from malnutrition and obstruction of the colon, failed to yield a potent fraction. This is the limit of our experience with human material.

*Obstruction of the Portal Vein*—Ellis<sup>3</sup> reported the presence of the toxic proteose fraction in the intestine of dogs dying of a thrombosis of the portal vein. The duration of the condition was not reported by him. We have searched for this material in the intestines of dogs dying from a complete or partial occlusion of the portal vein, with the idea of determining how rapidly this material may appear in the intestinal tract in quantities sufficient to give symptoms. The intestine of one dog dying in two hours after complete portal obstruction yielded a lethal amount for a dog weighing 7 Kg. The material from a dog with a similar condition which died in one hour failed to yield a fraction of definite toxicity. The large mesenteric vein was ligated in a dog and caused death in four and a half hours. The fraction prepared from this animal's intestine caused only mild toxemia. The material from the intestine removed from a dog after a partial but effective occlusion of the portal vein of five hours' duration caused a definite but not fatal intoxication in a small dog. On the whole, these results seem to indicate that an interference with the blood supply to the intestine causes a greater quantity of the toxic fraction to appear in the intestine. However, the quantity was less than that found in the intestine from dogs dying in about the same time from injection of proteose. It is possible that the large amounts of bloody exudate into the intestines, as the result of portal ligation may have lessened the quantity of material isolated.

*Histaminic Shock*—The fractions prepared from intestines of dogs which had received shock doses of histamine for several hours did not appear to be more toxic than the fractions prepared from normal intestine.

*Spleen*—We failed to isolate a fraction of appreciable toxicity from 20 Gm. of spleen allowed to autolyze in phosphate buffer for ninety hours. However, when aliquot portions were inoculated with the contents from the lower part of the ileum and anaerobically incubated for ninety hours they yielded a lethal dose of this fraction.

*Liver* —We have been able to obtain a lethal dose of this fraction from the liver of dogs in some instances. In other cases only a slight reaction was noted. We are unable to account for these apparent inconsistencies.

*Tissue Autolysis and Anaerobic Putrefaction* —When muscle, intestinal mucosa or spleen in quantities of from 10 to 40 Gm. were allowed to undergo autolysis in a buffered phosphate solution for periods of from twenty-four to ninety hours at 38 C., we were unable to demonstrate the presence of appreciable amounts of this toxic fraction. However, when aliquot portions of these substances were inoculated with the contents of the lower part of the ileum and incubated anaerobically as stated, we were invariably able to isolate a fraction which caused severe intoxication and death of the animals that were given injections. The symptoms, changes in the blood and pathologic processes were indistinguishable from those noted in animals that were given injections with material obtained from an obstructed intestine.

#### COMMENT

Our experiments show that a toxic proteose fraction could be isolated from material from various sources. The quantity of material obtained from each source was too limited to permit a detailed study of its chemical and physical properties. The effects produced by the injection of this material were the same regardless of its source. The symptoms and pathologic changes were for the most part typical of those noted in the animals dying from acute intestinal obstruction. The most noteworthy exception was the behavior of the blood chlorides. The whole blood and plasma chlorides were usually somewhat lowered. However, some animals in a condition of severe intoxication showed no change in blood chloride concentration. The latter is in harmony with the observations of Haden and Orr<sup>6</sup> that proteose fractions prepared from the content of obstructed intestine may cause little change in blood chlorides.

We believe that the failure of other investigators to obtain a toxic proteose fraction from normal intestine and other sources was due to the fact that they worked with too small a quantity of material. Thus the material obtained from the small intestine of one normal animal may cause such a mild reaction that it might be regarded as nontoxic, while the compounding of three or four such portions may represent a lethal dose. The absence of any easily detectable biologic reaction other than the determination of the lethal dose for dogs make progress in this direction slow and difficult. It is also to be recognized that the isolation of

<sup>6</sup> Haden, R. L. and Orr, T. G. The Blood Chlorides in Proteose Intoxication. *J. Exper. Med.* 48: 639, 1928.

this material is by no means quantitative. The possibilities of a loss of material due to destruction and adsorption by inert material are great.

Our experiments are not conclusive as to whether the proteose fraction is bacterial or nonbacterial in origin. The fact that bacteria or their products may have been present in all the material from which we isolated the toxic fraction, and that it was possible to increase greatly the yield of this material by anaerobic autolysis in the presence of the intestinal flora may be interpreted as indicating a bacterial origin. On the contrary, it is hard to explain its rapid accumulation in the intestine of animals after ligation of the portal vein or poisoning with a lethal dose on the basis of bacterial activity alone. It is well recognized that antiseptic autolysis *in vitro* may proceed differently from autolysis *in vivo*. Crucial evidence on this point might be obtained if sufficient quantities of sterile tissue were available. The observations of Towner<sup>7</sup> and of Ellis and Dragstedt<sup>8</sup> would indicate that it is difficult to obtain such tissues as pancreas and liver, completely sterile.

We believe our experiments indicate that the presence of a toxic proteose fraction in the intestine in various pathologic conditions should be regarded as merely an increase in the concentration of substances usually present in the intestine of healthy animals.

#### SUMMARY

A toxic proteose fraction has been isolated from normal intestine, obstructed small and large intestine, intestine of animals with obstruction of the portal vein and liver and from tissue allowed to undergo anaerobic autolysis in the presence of intestinal flora. The presence of this fraction was determined by the symptoms, changes in the blood and pathologic processes produced by its injection into dogs. It is suggested that the presence of this toxic material in various pathologic conditions should be regarded as indicating increased amounts of a material normally present rather than the elaboration of a new and specific substance.

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7 Towner, L. E. The Pathogenic Physiology of Experimental Gangrenous Pancreatitis, *J. A. M. A.* **86** 1112 (April 10) 1926.

8 Ellis, J. C., and Dragstedt, L. R. Effect of Liver Autolysis *in Vivo*. Preliminary Report, *Proc. Soc. Exper. Biol. & Med.* **26** 304, 1929.

# A REVIEW OF UROLOGIC SURGERY\*

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## KIDNEY

*Stone*—To the various types of urinary calculi usually described in the literature Braasch<sup>1</sup> added another form of lithiasis which is not generally recognized and which from its nature may be termed “hysterical lithiasis” This unusual demonstration of an abnormal psychologic process is manifested by symptoms simulating those of acute renal colic In order to make the deception complete a stone will be produced by the patient shortly after the colic, which on casual observation may be mistaken for renal calculus Nine cases of this unusual form of hysteria have been recorded at the Mayo Clinic, eight of these patients were women All gave a history of having passed urinary calculi repeatedly, one patient claimed to have passed more than 200 stones Examination of the specimens invariably showed the presence of inorganic material which made the diagnosis of foreign body certain Three of the patients were morphine addicts Sympathy and attention obtained through invalidism were evidently major factors in the other cases One patient secured prescriptions for alcohol in this manner All of these patients denied inserting the stones but when confronted with the chemical analysis all but one patient admitted the accusation

Another unusual type of urinary stone mentioned is that which occasionally is observed as causing hematuria Gross calculi are not found on surgical exploration of the kidney Microscopic examination

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\* Submitted for publication Aug 14 1930

<sup>1</sup> Braasch W F Unusual Types of Urinary Lithiasis J Urol **23** 1 (Jan) 1930

of the kidney will disclose the presence of numerous minute calculi in the renal tubules, which are moderately dilated. Such calculi may occur secondary to obstruction from blood clots accompanying an essential type of hematuria although it would seem more probable that the calculi were an etiologic factor of the hematuria.

Hunt<sup>2</sup> in considering some of the problems arising in the treatment for lithiasis, renal tuberculosis and neoplastic disease, stated that lithiasis is the most common surgical lesion in the kidney. During recent years at the Mayo Clinic, approximately 50 per cent of the operations performed on the kidney have been for calculus. The renal cause of lithiasis has not as yet been determined. The hypothesis that remote foci of infection are instrumental in the development of lithiasis has received much support. Other evidence tends to indicate that chemical changes incident to the advent of bacterial invasion of the kidney and urine may be instrumental in the precipitation and agglutination of the normal constituents of urine. Stones in the kidney are multiple in more than 40 per cent of the cases and are bilateral in approximately 10 per cent. At times stones in the kidney are associated with calculi in one or both ureters, which complicate the determination of proper methods of treatment. The significance of the complications of infection, urinary obstruction and destruction of renal function is emphasized by the frequency with which nephrectomy is necessary in treating renal lithiasis, an incidence so high as to reflect unfavorably on conservative non-operative methods. At the Mayo Clinic, in a recent review of 941 cases in which operation was performed for renal calculus, nephrectomy was necessary in 334 cases (35 per cent) owing to infection and destruction of renal tissue. If a renal stone has not produced subjective symptoms and is less than about 0.5 cm. in diameter, its removal is not especially urgent. It should be given an opportunity to pass spontaneously. If after observation for a certain period, the position does not change but the size increases, early removal should be considered. Repeated renal colic from a calculus of considerable size retaining its position in the kidney is sufficient indication for removal. Another exception to the rule that renal calculi should be removed surgically when the diagnosis is established is when the condition occurs in aged patients without apparent symptoms and without diminution in renal function. If branched stones are causing symptoms and injury to the kidney, the choice of conservative removal or nephrectomy is not always easy to determine. In the presence of adequate renal function conservative removal of the stone is the method of choice. Nephrectomy is easier in cases of large branched stones but conservation of renal tissue under such difficulties is possible in the hands of a skilled surgeon.

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<sup>2</sup> Hunt, V. C. Problems Related to Surgical Lesions of the Kidney. *Ann Surg* 91:92 (Jan) 1930.

In cases of ureteral lithiasis associated with renal stone, it is not always possible to determine the amount of infection and of renal function previous to removal of the ureteral calculus, particularly if the ureter will not permit the passage of a catheter. It may be best to remove the ureteral calculus first if it is situated in the lower half of the ureter, and to determine the renal function and degree of infection later. If a ureteral stone is situated in the upper half of the ureter, it may be removed simultaneously with the calculus from the kidney through a posterior incision, if a conservative operation can be accomplished, or simultaneously with nephrectomy, if the radical operation is indicated. In case of the latter procedure, nephro-ureterectomy to below the ureteral stone has proved the method of choice.

Bilaterality of renal lithiasis is serious in proportion to the amount of renal injury and infection. It has seemed best to operate first on the side to which acute symptoms have been referable. In the absence of acute symptoms but with difference in function of the two kidneys, operation on the kidney with the better function is preferable.

Hunt has found it possible to remove stones by pelvolithotomy in 85 per cent of cases. This operation has been reserved for cases in which the stones are inaccessible through the pelvis because they are encysted in the terminal calices and situated rather superficially under the renal capsule. In the series of 941 cases of lithiasis there were 15 deaths, a mortality of 1.6 per cent. The mortality rate in 607 cases in which conservative operations were performed was 1.3 per cent as opposed to 2.1 per cent in cases in which nephrectomy was performed.

The upper part of the urinary tract seldom is alone the site of tuberculosis, and primary tuberculosis of the urinary tract rarely if ever occurs. It is generally accepted that tuberculosis of any part of the genito-urinary tract is hematogenous in origin. To determine the incidence of bilaterality of renal tuberculosis at the Mayo Clinic a review was made of the operative and nonoperative cases during a ten year period. During this time nephrectomy was done on 574 patients and 264 patients were observed on whom operation was not performed. In the latter group the diagnosis of renal tuberculosis was definitely established and all of the cases were considered nonsurgical with the exception of 43 patients who refused nephrectomy. Approximately 73 per cent of the cases of renal tuberculosis were regarded as suitable for nephrectomy. The 221 cases were considered nonsurgical because of bilaterality in 77, occlusion and relative freedom from symptoms in 48, active and advanced pulmonary tuberculosis in 37, and extensive and advanced tuberculosis elsewhere in 38. In 10 cases in which nephrectomy had been performed for tuberculosis of one kidney tuberculosis of the remaining kidney was found in 4 nonoperative cases. Bilateral renal tuberculosis was proved at necropsy. The diag-



nosis of bilaterality in the 77 cases was definitely established in most instances through the presence of bacilli of tuberculosis in the secretion from both kidneys or through inoculation of guinea-pigs. Definite evidence of bilateral renal tuberculosis existed in 91 of the nonoperative cases. Among those cases in which nephrectomy was performed, evidence of bilaterality existed in 20. There were 14 deaths (2.4 per cent) in the series of 574 cases in which nephrectomy was performed for renal tuberculosis, in the last 357 cases there were only 7 deaths (1.9 per cent). In general, there has been a mortality of 20 per cent within five years, with partial recovery of 80 per cent of the patients, 60 per cent have been completely cured, and 20 per cent have had persisting vesical symptoms. The shorter the duration of the disease and the less extensive the renal involvement and cystitis, the better will be the result. Braasch recently reviewed 65 cases in which nephrectomy was done between five and fifteen years ago and in which advanced secondary ulcerative cystitis was present with markedly reduced capacity of the bladder. Among these there was a five year mortality of 37 per cent. The condition of the bladders of 30 per cent of patients who were living was not improved. Early nephrectomy, before advanced involvement of the bladder occurs, insures more satisfactory results than may be expected in cases in which there is advanced involvement of the genito-urinary tract.

Most malignant lesions of the kidney tend to metastasize rapidly through local extension to perirenal structures and to the renal vein, which provides direct paths for remote metastasis. In the absence of demonstrable metastasis and fixation of the kidney by direct extension to surrounding structures, nephrectomy affords the best prognosis. The anterior transperitoneal route facilitates removal of large tumors entirely inaccessible through the usual posterior incision.

*Hydronephrosis*—Stevens<sup>3</sup> presented a series of twenty-three cases in which surgical treatment was given for obstruction at the uretero-pelvic juncture. In twenty of these cases the condition could probably have been corrected by operation with preservation of the kidney if a correct diagnosis had been made early. The most common obstruction at the ureteropelvic juncture is that caused by aberrant vessels going to the lower pole of the kidney. Some degree of ptosis of the kidney may be necessary before these vessels will interfere with the free flow of urine in the ureter. The anomalous vessels may be anterior to the surface of the kidney. In five of seven cases in which the condition was noted the vessels passed anterior to the ureter, and in two, posterior. In the series of twenty-three cases there were thirteen of hydro-

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3 Stevens A. R. Hydronephrosis Due to Obstruction at the Uretero-Pelvic Junction. *J. Urol.* 23: 493 (May) 1930.

nephrosis due to aberrant vessels Nephrectomy was done in ten One patient had had symptoms for one week, another for two years and the remainder of the patients from ten to twenty-three years In all cases there was little if any function from the hydronephrotic kidney In seven cases infection was proved to be present before operation The kidneys in all of these cases were greatly enlarged with thin and scanty parenchyma In eight of the ten cases nephrectomy was performed on the left side There was an equal number of men and women in the group, but in the latter the large kidney was always on the left side There were four cases of obstruction from dense fibrous encapsulation of the ureteropelvic region Careful search did not reveal any other factor In three of the four cases, the corresponding kidneys were infected at the time of operation, and the peripelvic fibrous tissue was probably of inflammatory origin Trauma accounted for the condition in the fourth case

Von Lichtenberg<sup>4</sup> stated that treatment of such an important structure as the kidney should be directed toward its conservation From his conception of conservative surgical intervention and his experience in treating what he called "urinary constipation," he concluded that in the treatment for this condition a conservative method may be used, having for its purpose the elimination of the symptoms and the maintenance or improvement of the remaining renal function A conservative procedure is indicated especially in all cases in which the condition is bilateral, or in which the other kidney is also injured and the conservation procedure is not contraindicated by infection A temporary fistula of the kidney assists essentially in the success of the operation The kidney must be sufficiently exposed to give a clear picture in situ This necessitates removal of the twelfth rib and occasionally of the eleventh rib The palliative procedure disconnects the pathogenic lesion whereas the radical operation removes it

[*Editorial Note*—In the last decade great strides have been made toward conservative renal surgery Partial resection of the kidney, plastic operation on the pelvis and ureters, the resection of obstructing anomalous vessels etc, have made nephrectomy a far less frequent operative procedure

In line with this conservative type of surgical intervention is the effort made by those who teach the doctrine of ureteral stricture as a cause of renal stasis and who advocate repeated ureteral dilatation as a means of establishing more satisfactory drainage of the tract The rationale of the latter procedure is still *sub judice*, and the subject is of caustic controversy Nevertheless, both ureteral dilatation and conservative operations on the kidney are procedures which illustrate

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<sup>4</sup> von Lichtenberg Hydronephrosis Am J Surg 7 747 (Dec) 1929

the definite trend toward making every effort to preserve functioning renal parenchyma whenever possible ]

Barringer<sup>5</sup> expressed the belief that there are two main reasons for conservatism in operating for hydronephrosis and hydropyonephrosis. First, present-day methods of examination are inadequate for determination of precisely what a kidney is doing. Second, it is not known how far a kidney is capable of returning to normal. An infected kidney can return to normal even if largely infected, but there is no standard by which it can be ascertained, prior to operation, what a kidney can do.

Walters<sup>6</sup> stated that a review of the literature on ureteropyelonephrostomy indicates that if the anastomosis is correctly made function will be satisfactory. He reported two cases in which anastomosis was successful. In these two cases lateral anastomosis was made between the ureter and the dependent portion of the hydronephrotic renal pelvis. A ureteral catheter was placed temporarily through the anastomosis to serve as a scaffolding for healing. In the first case the catheter had been inserted in the ureter in order to decompress the renal pelvis and was there at the time of operation. It was carried into the pelvis through the anastomosis and maintained in place for twenty days, when it was removed. Temporary nephrostomy was done in this case to prevent tension at the point of anastomosis. A no. 14 French catheter was used, which was removed on the eighth day. In the second case the cause of the obstruction was a dense scar of fibrous tissue at the ureteropelvic juncture. Connective tissue had extended to a point below this angulating the ureter. When first exposed this angulation appeared to be the site of obstruction. After it was free, an opening was made in the ureter about 3 cm. distal to this point and a catheter was pushed toward the renal pelvis as a probe. It was then found that the obstruction had not been relieved but existed at the ureteropelvic juncture. When the ureter was dissected to this point the obstruction was found and a lateral anastomosis was made between the ureter below and the pelvis above. A ureteral catheter was carried through the anastomosis and out of the incision through the ureterostomy opening in which it was left for thirteen days. A nephrostomy tube was also used and removed on the tenth day following operation.

Hirst<sup>7</sup> summarized present knowledge of the kidney in cases of pregnancy and presented certain additional information. The title is

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5 Barringer B. S. Discussion of Hydronephrosis, *Am J Surg* **7** 752 (Dec) 1929.

6 Walters Waltman. Ureteropyelonephrostomy for Urinary Obstruction at the Uretero Pelvic Junction. *Ann Surg* **91** 101 (Jan) 1930.

7 Hirst I. C. The Kidney of Pregnancy. *Am J Obst & Gynec* **18** 528 (Oct) 1929.

used in a broad sense to include (1) the diagnosis of hydronephrosis, infected hydronephrosis and pyelitis complicating pregnancy, with the comparison of the relative frequency of appendicitis and disease of the gallbladder, (2) the relation of hydronephrosis and pyelitis to early and to late gestational toxemia, (3) differential tests of renal function and pyelograms to discover additional factors in the cause of the common hydronephrosis in pregnancy, with special attention to the possibility of ureteral edema or chronic passive congestion that might be a contributing cause of late gestational toxemia and eclampsia, and (4) an attempt to differentiate renal and hepatic toxemia of pregnancy by the effect of the administration of a blood pressure lowering preparation from liver

From his review of important articles on the subject, and from his own experience Hirst concluded (1) cystoscopic urologic diagnosis is of significance in obstetric service and, when carefully performed no risk is involved, (2) vasodilatation and circulatory stasis of the distal ureter may directly or indirectly be concerned with late gestational toxemia, (3) early and late toxemia are essentially different, the latter being primarily renal in origin, and (4) the liver preparation appears to bear insufficient specific action to separate a hepatic type from the late forms of the toxemias of pregnancy

From a summary of data concerning ninety-seven obstetric patients who were subjected to cystoscopic and pyelographic examinations, the following significant facts were obtained Ureteral obstruction appeared only four times, the absence of frequent obstruction presupposes some additional factor responsible for impaired drainage not accounted for by atonic ureteral dilatation or latent infection so common in pregnancy The impairment is believed to be circulatory in the form of intermittent vasodilatation or chronic passive congestion around the distal ureter, evidenced by edema of the orifice in the form of irregularity of shape and puffing Jaundice did not appear in any case but in one instance subacute exacerbation of a chronic cholecystitis followed ureteral catheterization Even if the renohepatic interrelation is of significance in infection and toxemia it appears that it is not particularly significant in a careful cystoscopic examination of the obstetric patient Other harmful results of urologic investigation included troublesome increases in severity of chronic pyelitis in two patients and in one patient it precipitated labor at term

*Pyonephrosis*—Paschkis<sup>8</sup> stated that epithelial changes in the urinary tract simulating cystitis cystica and glandularis are rare and their etiology is unknown The inference is that there are stimuli of

<sup>8</sup> Paschkis Rudolf Pyonephrose mit Ureteritis cystica Ztschr f urol Chir  
28 64 1929

various types which cause an otherwise normally functioning gland or cyst to develop to an advanced stage. In other cases such stimuli may cause epidermization of the mucous membrane. Paschkis observed cases of renal calculi in which the mucous membrane has presented a condition known as pyelitis glandularis.

The case of a woman, aged 55, who had right-sided colic with disturbances of the bladder, was reported. A history of hematuria and of trauma of the right side of the abdomen was obtained. Twenty-four years before, following a forceps delivery, a perinephritic abscess developed on the right side and was drained. Examination revealed closed right pyonephrosis. Intracapsular nephrectomy was performed. Pathologic examination of the kidney showed pyonephrosis. Chronic cystic proliferating ureteritis almost obliterating the lumen was found in the upper part of the ureter. Paschkis concluded that in childhood hydrohematonephrosis may have formed due to the injury, later, infection ensued causing both the pyonephrosis and the perinephritic abscess.

*Lipomatosis*—Kutzmann<sup>9</sup> found that replacement lipomatosis of the kidney is of rare occurrence. He cited the case of a man, aged 56, who complained of continuous dull pain in the region of the right kidney, dysuria and frequency. A diagnosis of right calculous pyonephrosis was made. Intracapsular nephrectomy was performed. The kidney was found to be markedly adherent to all structures in the lumbar region, especially to the posterior peritoneum and diaphragm. The perirenal fat was fibrous and tough. These factors greatly hindered freeing the kidney from the adjacent structures and made the intracapsular procedure imperative. Nephrolithiasis, chronic diffuse nephritis, atrophy of the renal parenchyma and fatty degeneration of the renal hilus, which apparently had invaded the kidney, were found. Recovery was uneventful.

Twenty-eight proved cases and nine doubtful cases were noted in the literature. Kutzmann concluded that replacement lipomatosis of the kidney is always associated with severe infection of the kidney. Calculous disease was associated in 71 per cent of the cases. The sexes and the side involved were about equal, pathognomonic signs or clinical symptoms were not apparent. The cases reported earlier were found at necropsy whereas those recently observed were found at operation. Treatment is directed to the associated condition and usually is nephrectomy. Such kidneys are painful, badly infected and functionless. The pathogenesis is hypothetical. The process of replacement is probably one of invasion of perirenal peripelvic and hilus fat along the large vessels through the renal hilus.

<sup>9</sup> Kutzmann, A. A. Replacement Lipomatosis of the Kidney, Proc Ninth Meeting Clin Soc Genito-Urin Surg, San Francisco July 1929.

[*Editorial Note*—Replacement of renal parenchyma by fat is of rare occurrence, and has been considered only occasionally in the American literature. The European literature however contains many hypothetic considerations concerning its unknown etiology and pathogenesis.]

The substitution of renal parenchyma by true adipose tissue has been variously designated in the literature as lipomatous nephritis, lipomatous paranephritis, lipoma diffusum renis, substitutio renis adiposa, lipomatosis renis, fatty transformation of the kidney, fat replacement of the kidney and fatty degeneration of the kidney. These terms are more descriptive of the latter stages of this pathologic anatomic process in which the entire parenchyma of the kidney may have disappeared. In the earlier stages in which the changes have not as yet occurred in the hilus and polar regions of the kidney the term "lipomatous paranephritis" has been considered more descriptive by certain observers. The process has not been satisfactorily explained. The condition is usually classified with the paranephritides. The fat either may surround the kidney or may limit itself to individual areas usually at the hilus or polar regions of the kidney. It may even involve the ureter, assuming colossal dimensions. The fat substitution usually parallels an atrophying renal process.

The theories concerning the pathogenesis of this condition may be placed in two essential groups: a minority of authors considers the primary growth to be from the fatty capsule while coincidentally the fat of the hilus forces its way into the kidney, leading secondarily to atrophy. There is no overwhelming evidence to support this view. The majority of authors holds that the substitution of fat is secondary and considers that the atrophying process is of primary importance. To support the latter view it has been pointed out that at times retroperitoneal lipomas assume huge proportions, surrounding and pressing the kidney on all sides and yet not causing destruction or atrophy of the parenchyma of the kidney. If the fatty growth were of a primary nature, histologic examination should reveal traces of renal tissue which has never been the case. Between the fat tissue and the remaining atrophic parenchyma of the kidney there is usually a sharp boundary.

Calculous disease of the kidney seems an important factor. Analysis of thirty-five cases revealed calculous disease in twenty-six (79 per cent), bilateral cases of replacement lipomatosis three cases and bilateral renal and ureteral calculi combined with an infection two cases. Destruction of the pelvis and parenchyma of the kidney and finally the familiar picture of pyonephrosis result. The presence of calculi and the chronicity of the infection may result in a proliferative and invasive power to the already hyperplastic peripelvic fat about the renal hilus and in a renal invasion around the large vessels.]

*Rupture*—Shapiro<sup>10</sup> stated that rupture of the kidney may result from direct trauma by which the kidney is driven against the lower ribs or against the transverse processes of the first and second lumbar vertebrae, from indirect trauma, from muscular action producing abrupt flexion such as jumping backward or dodging objects, or it may occur spontaneously. The seriousness of rupture of the kidney depends mainly on the extent and site of the injury. A subcapsular rupture, after a few days of pain in the loin associated with hematuria, will entirely disappear. In this type of rupture there is a tearing of renal tissue, but the capsule remains intact. From the injured tissue there is an outpouring of blood and urine, with the result that the intracapsular volume increases and with it the intracapsular pressure rises also. A total rupture with severance of the main vessels will rapidly exsanguinate the patient, or, with a torn peritoneum, extravasation of urine into the peritoneal cavity will result in fatal peritonitis. The blood and urine escape through the torn capsule of the kidney into the retrorenal tissue between the kidney and the peritoneum, forming a mass of varying size and composed of a mixture of blood and urine.

A bleeding kidney is evidenced clinically not only by hematuria but by ecchymosis, or subcutaneous hemorrhage. The latter is usually found in the flank and may prove a valuable aid in diagnosis. The cardinal symptoms of ruptured kidney are pain of varying degrees, tumor and hemorrhage, together with the condition of shock. The pain is usually in the loin but may radiate down the thigh, to the penis and scrotum.

Secondary hemorrhage has sometimes followed rupture after the patient has apparently recovered from the injury. Other sequelae of rupture of the kidney are suppuration, calculi and cysts, and even nephritis and malignant neoplasms have been reported.

In any treatment for ruptured kidney attempts should be made to conserve the function of both kidneys. The majority of such injuries will heal by expectant treatment. Whether operation is necessary will be determined by the extent of bleeding. Surgical intervention is indicated when there is a gradual rise in the pulse rate and a sharp drop of the erythrocytes, the hemoglobin and the blood pressure. Conservative procedures of tamponade, suture or drainage should be carried out if the bleeding is such that a tampon will check it, if the kidney is only slightly injured or if the fragments can readily be approximated by suture. If the bleeding is uncontrollable, if the tear in the kidney cannot be sutured successfully, if the artery and vein are shorn off, if the pelvis is severely torn or if the ureter is entirely severed, nephrectomy is indicated. Removal of the kidney is also indicated if

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10 Shapiro E. Z. Ruptured Kidney. *J Urol* 23: 343 (March) 1930.

the rupture is associated with severe infection or disease such as hydronephrosis and calculi. Laparotomy is urgent if there is suspicion of torn peritoneum or injury of the abdominal viscera.

*Perirenal Tumors*—Crabtree<sup>11</sup> stated that perirenal lipomas and true fatty tumors of the urinary organs are to be distinguished from the lipomatous changes of chronic infections. Perirenal fatty tumors are more common than renal lipomas. They form two definite groups, one in which long-standing tumors by their size produce symptoms of pressure, the other tumors in which the clinical picture is suggestive of malignancy. Pathologically these fatty tumors range between normal fibrous fat and sarcoma. In the pure lipomas the blood supply to the tumor is meager and the fibrous capsule incloses the tumor in such a way that surgical enucleation of a large mass is not difficult. Lipoma of the perirenal and retroperitoneal area is more common in women. The disease seems independent of associated organs and occurs with equal frequency on either side. In some cases a history of injury is given. In other cases of long standing the tumor grows rapidly after injury or some form of irritation such as inflammation of the appendix or colitis or for no apparent reason.

The most common symptom is enlargement of the abdomen, often symmetrical. Since the fat is soft at body temperature the tumor is not definitely localized, a phenomenon which often leads to the diagnosis of ascites, this sometimes occurs even though the tumor is growing rapidly. The apparently normal fat content is not available for metabolism in these patients. In some of the cases studied loss of weight was rapid although the tumor was not sufficiently large to produce derangements of physiology due to pressure.

The majority of cases reported have been diagnosed only at operation or at necropsy. Deformity of the kidney has not been recorded, but it has become displaced from pressure or its pelvic outline appears normal. Braasch's statement that when the outline of the pelvis is normal it is not likely that the surrounding tumor is of renal origin is confirmed in these cases. Whenever possible, operation is the treatment of choice. In cases of pure lipoma in which the lobulated masses are encapsulated, the mass, even though large, is often easily removed. These cases are usually not good surgical risks. Wahlendorf found an immediate mortality of 25 per cent in a series of 165 cases, other observers report a similar mortality rate. In many cases in which the patients survived operation, complete removal of the tumor had not been accomplished. Repeated operations were not well tolerated. Data are not available to determine longevity in those cases in which operation was incomplete or was not performed.

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<sup>11</sup> Crabtree, E. G. Perirenal Lipoma with Generalized Abdominal Lipomatosis, *J. Urol.* **23** 545 (May) 1930.



MacKenzie<sup>12</sup> reported a case of spontaneous perirenal hemorrhage occurring in a man suffering from polycythemia. Nephrectomy was performed, and the patient recovered.

Sixty-six cases of perirenal hematoma have been reported in the literature, but none has occurred in conjunction with polycythemia. Four have occurred in patients who had hemophilia. Spontaneous perirenal hemorrhage has been classified according to the source, such as primary, of unknown etiology, and secondary due to some discoverable lesion.

#### BLADDER

*Reflux*.—Bronner and Schuller<sup>13</sup> stated that the vesico-ureteral or vesicorenal reflux is variously described in the literature as a vesico-renal backflow, forced ureters or gaping of the ureters. The lesion never occurs under normal conditions because of the valvelike action of the ureteral orifice. As soon as there is disturbance of the physiologic function of the bladder and ureters, the valvelike action of the ureteral orifice ceases and a vesico-ureteral or a vesicorenal reflux ensues. Conditions leading to disturbance in the action of the ureteral orifice are marked hypertonia of the musculature of the bladder due to tenesmus in different diseases, disturbances due to narcosis or lumbar anesthesia and ureteral rigidity in certain inflammatory conditions, leading to the so-called funnel-shaped orifice.

The case of a girl, aged 24 years, who had diffuse tuberculous cystitis and left renal tuberculosis in which a vesicorenal reflux developed on the opposite side, was reported. The first stage of the vesicorenal reflux of the right side was observed previous to operation, and it was thought that nephrectomy on the left side would cause the condition to disappear. To check up, cystograms made fourteen days, one month and one and a half months, and again fifteen months later, showed gradual progression of the vesicorenal reflux to complete hydronephrosis. The patient was observed during the entire course of the disease, and it was possible to study the various stages of vesicorenal reflux. First there was only slight dilatation of the lower portion of the ureter with the urine entering this part of the ureter. Later the urine entered as high as the pelvis of the kidney and there was progressive dilatation of the entire ureter. In the third stage, tortuosity with occasional kinking of the ureter developed, leading to retention of the urine in the upper portion of the ureter and pelvis of the kidney. The final stage of the disease was marked by hydronephrosis.

12 MacKenzie D. W. Perirenal Hematoma Primary with Polycythemia, *J Urol* **23** 535 (May) 1930.

13 Bronner H. and Schuller, H. Der Blasen-Nierenruckfluss (Vesico-renal Reflux), Klinische und röntgenologischen Beiträge, *Fortschr a d Geb d Röntgenstrahlen* **40** 419 (Sept.) 1929.

The symptoms are in accordance with the various stages of the disease. First there is only a drawing sensation in the lower part of the back, then the sudden desire to urinate develops, especially noticeable on a change from the horizontal to the vertical position. It often develops into urinary incontinence. In the final stage, urination in two or several periods follows. The latter is due to the fact that during actual micturition the bladder expels the urine both into the urethra and toward the kidney.

Cystoscopy is the method of examination in vesicorenal reflux. The direct application of pyelography is contraindicated since the slightest pressure may lead to the opaque substance entering the venous system of the kidney. Among opaque mediums are a 12 per cent solution of sodium iodide or a 5 per cent solution of iodized oil.

The various diseases leading to vesicorenal reflux are: (1) Tuberculosis of the bladder and kidney. According to Bumpus, this is responsible for 40 per cent of all reflux and appears in 20 per cent of all cases of tuberculosis of the kidney, occasionally it may disappear spontaneously following removal of the diseased kidney or conservative treatment of the bladder. (2) Infections of the bladder or of the pelvis of the kidney. Reflux of this type is relatively benign and as a rule it disappears as the result of conservative treatment. (3) Conditions associated with retention of long standing, such as ureteral stricture and hypertrophy of the prostate. It has been noted by Bumpus that the vesicorenal reflux which accompanies enlarged prostate glands increases from 4.74 to 11.42 per cent following prostatectomy. (4) Implantation of the ureters into the colon as practiced in certain operations. Maydl's attempt to transplant the entire trigone of the bladder into the colon so as to prevent the reflux has not led to better results. From 70 to 80 per cent of all colonic transplantations of the ureters result in renal reflux, necessitating later the removal of the kidney. (5) Transvesical resection of enlargements of the lower portion of the ureter. (6) Certain instances of ureteral stones, producing partial obstruction. (7) Certain lesions of the spinal cord and exceptional congenital lesions.

Whether or not vesicorenal reflux always leads to insufficiency of the affected kidney is not definitely determined.

Teposu<sup>14</sup> described two cases of vesicorenal reflux. The first case occurred in a man, aged 55, who since 1916 had complained of symptoms referable to the bladder, and who in 1925 and 1926 had had three successive operations. A diagnosis of sclerosis of the trigone (due

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<sup>14</sup> Teposu, E. Insuficienta orificiului ureteral și reflux vesico-renal, *Cluj med* 10 579, 1929.

to scarifications from the operations) was made, and it was thought that this sclerosis was responsible for the vesicoenel reflux. Following the excision of the trigone, the lesion apparently healed. The second case was that of a girl aged 14 years. The cause was not definite. The vesicoenel reflux was confined to the left side.

In connection with these two cases, Teposu considered the mechanism of vesicoenel reflux and arrived at the conclusion that it may be the result of the following three factors: (1) disturbance in the normal peristalsis of the ureter, (2) disturbances in the obliquity of the intramural portion of the ureter, and (3) insufficiency of the valvular function of the ureteral orifice.

The conditions that may lead to disturbance of the foregoing factors are acute or chronic inflammation, tuberculosis, lesions of the trigone, ureterocystoneostoma, prostatic hypertrophy, diseases of the nervous system (tabes dorsalis, poliomyelitis, multiple sclerosis) and spina bifida.

*Tumors*—McCarthy<sup>15</sup> stated that in consideration of any technic in the treatment for new growths occurring in the bladder, diagnosis is the basic question. Precise diagnosis is necessary not only prior to operation, but by free mobilization at the time of operation. In cystoscopic transurethral and transvesical diathermy there should be a wider application with the largest possible electrodes. Results from radium and the application of deep roentgen rays have not been satisfactory, and their use is no longer advocated. Free mobilization of the bladder is advised as a preliminary step in cases in which open operation is performed. If all these measures fail, prompt cystectomy should be done.

*Carcinoma*—Fey and Bompart<sup>16</sup> reviewed 108 cases from the literature of total cystectomy for carcinoma of the bladder. Baidenheuer performed the first operation of this type. The immediate results were not encouraging. Fifty-six (51.8 per cent) of the 108 patients died early. In all cases in which the ureter was placed in the urethra, and in 59 per cent of cases in which the ureter was transplanted to the intestine, the patients died. Transplantation into the vagina was followed by a mortality of 33 per cent. Cutaneous ureterostomy resulted in a mortality of 23 per cent. Eighty-five patients were operated on by a one-stage method, 50 (59 per cent) died. Twenty-three patients were operated on by the two-stage method, 6 (26 per cent) died. The late results of total cystectomy are not satisfactory.

15 McCarthy J F. A Consideration of Technique in the Management of New Growths of the Bladder. *J Urol* 23:323 (March) 1930.

16 Fey B. and Bompart H. A propos de la cystectomie totale pour cancer de la vessie. *Paris med* 2:359 (Oct 19) 1929.

The mortality is approximately 30 per cent for the first six months after operation, 40 per cent for the first year and 70 per cent for the first two years.

Fey and Bompert stated that cystectomy for carcinoma has received unjustified discredit at the present time. Carried out under certain conditions such as early operation by the two-stage procedure and iliac ureterostomy, this operation would give results superior to those in use at the present time. The authors are of the opinion that this method will some day be the treatment of choice for carcinoma of the bladder.

*Hernia*—Wakeley<sup>17</sup> stated that it is possible for the bladder to protrude through any of the hernial orifices, although the protrusion usually is inguinal or femoral. Inguinal hernia of the bladder is less common in women than in men, whereas femoral hernia of the bladder occurs almost solely in women. Of forty-two cases of the femoral variety, forty occurred in women. Hernia of the bladder may be classified as extraperitoneal, paraperitoneal and intraperitoneal, according to the relationship of the hernia to the peritoneum. In extraperitoneal hernia of the bladder the anterior or lateral extraperitoneal surface of the bladder enters the inguinal or crural canal. It is always small and rarely gives rise to symptoms. It takes the form of a direct inguinal hernia. In paraperitoneal hernia of the bladder the hernia may be direct or indirect, the bladder always lies on the inner side of the hernial sac. The serous covering of the superior surface of the bladder will form the inner wall of the peritoneal sac. It is the most common of the three varieties and the easiest to treat successfully. The bladder is usually situated at the inner and posterior part of the peritoneal sac. During operation, when the sac is dissected from the constituents of the spermatic cord, a definite increase in the thickness of the sac will be observed, and careful gauze dissection will demonstrate the adherent bladder. Intraperitoneal hernia of the bladder is a rare condition, but is more common than that of the extraperitoneal variety. In Wakeley's series of forty cases, it occurred in fourteen. These hernias usually are large, secondary in origin and practically always in the inguinal region. There is a complete hernial sac, and the upper and posterior part of the bladder enters the sac, which is external to the deep epigastric artery. Frequently the hernial sac contains, besides the bladder, loops of small and large intestine and omentum.

Any factor which increases the volume of the bladder favors hernia of the bladder, consequently stricture of the urethra and prostatic

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<sup>17</sup> Wakeley, C. P. G. *Hernia of the Bladder—Its Etiology and Treatment*. Brit. J. Urol. 2:1 (March) 1930.

enlargement are predisposing factors in old men, and a tight prepuce or a pinhole meatus may be considered predisposing factors in infants. Pregnancy is the most common predisposing factor in women. In the male the bladder is in closer relationship with the internal inguinal fossae and hernia of the bladder is more often associated with direct than with oblique inguinal hernia. In aged patients the hernia is likely to be large, owing to relaxation of the musculature of the abdominal wall and muscular atony of the bladder.

When a paraperitoneal hernia of the bladder is discovered during operation, the treatment should vary according to the size of the hernia and its relation to the sac. If the hernia is small, it can be separated from the peritoneal sac by gauze dissection and invaginated into the abdomen, a purse-string suture being inserted through the floor of the inguinal canal to prevent recurrence. If the peritoneal sac covers a considerable portion of the bladder it should not be stripped off, excision should be performed around the bladder attachment on the inside, going up as high as the abdominal ring on the outside where the sac is quite free. The bladder is then invaginated and kept in place by a purse-string suture. Should the floor of the inguinal canal prove to be too weak and recurrence is expected, a flap from the anterior sheath of the rectus muscles may be turned outward and sutured to the internal oblique muscle. After taking care of the vesical hernia, operation is performed for the inguinal or femoral hernia.

*Cystitis*—Mills<sup>18</sup> found few reports in the literature of gas-containing cysts or vesicles in the wall of the urinary bladder of the human being. Cystitis emphysematosa is a pathologic entity, being a localized lesion confined to the inner layers of the wall of the bladder and not a part of a generalized gas-producing bacterial infection. The name indicates an inflammatory condition of the bladder associated with the presence of gas vesicles in the tissues.

Mills reported three cases of cystitis emphysematosa occurring in men, disposing of the previously assumed limitation of this disease to women. The last cystoscopic examination of one patient was performed about four months before death, had cystitis emphysematosa existed at that time it might have been recognized. The other two patients did not present urinary symptoms for which a cystoscopy would have been indicated. The presence of marked evidence of both acute and chronic cystitis and of recent and old hemorrhage indicated that cystitis had existed for a considerable time before death.

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18 Mills, R. G. Cystitis Emphysematosa. I. Report of Cases in Men, *J. Urol.* 23: 289 (March) 1930.

*Drainage*—Lowsley<sup>19</sup> stated that suprapubic cystostomy as a preliminary procedure in preparing for a more radical operation has a definite value in surgery. The mortality rate is unusually low in cases in which preliminary drainage is done, considering the age and poor general condition of the patients on whom operations have been performed. This is particularly true in cases in which the prostate gland is enlarged and retention of urine is complete or partial. He noted that in many cases of prostatic enlargement the patients had received considerable trauma from attempts to pass instruments. In a few cases obstruction was so severe as to require evacuation of the bladder by immediate suprapubic cystostomy in preference to further attempts at intra-urethral manipulation, even though gradual decompression of the overdistended bladder is desirable whenever feasible.

There were 34 deaths (8.9 per cent) in 381 cases in which the bladder was drained as a preliminary to prostatectomy for benign hypertrophy. Fifty per cent of the deaths occurred in men aged more than 70 years, 6 of whom were more than 80. The youngest man who died was 50 and the oldest was 89, the average being 69.5 years. Death occurred after from one day to thirty-nine days, the average time being twelve and five-tenths days.

Kaufman<sup>20</sup> reviewed 300 diversified cases in order to study the use of the catheter in postoperative retention of urine. The incidence of retention was 17 per cent in these cases. The incidence of retention was highest following operations on pelvic and abdominal organs, varying from 18 per cent in operations for hernia to 31 per cent for hysterectomy. In a total of 34 abdominal operations, including operation on the gallbladder, stomach, appendix and large and small intestines, catheterization was performed on 23.5 per cent of the patients. In most cases the interval between operation and catheterization was twelve hours.

When a catheter is employed as a routine for postoperative retention, a urinary antiseptic should always be given as soon afterward as possible, and should be continued for at least from three to four days after catheterization ceases. A single catheterization does not require irrigation or instillation, but repetition over more than two or three days requires instillation once a day of either silver nitrate, 1:2,000, or acriflavine, 1:2,000, ½ ounce (14.175 Gm.). If it is necessary to

19 Lowsley, O. S. Preliminary Drainage in Cases of Vesical Obstruction with Particular Reference to Stricture of the Urethra, *J. Urol.* **23**: 307 (March) 1930.

20 Kaufman, L. R. Use of the Catheter in Retention, *Am. J. Surg.* **7**: 785 (Dec.) 1929.

who twelve years previously had had an accident in which the knife blade entered in the region of the hip, broke off and could not be found afterward

Litholapaxy is not a satisfactory procedure in cases in which the foreign body consists of metal, glass or bone and forms the nucleus of a stone, or when composed of softer substances such as wood, india rubber, chewing gum and paraffin owing to the difficulty in disintegrating and evacuating the nucleus. Some of the foreign bodies float to the top of the fluid in the bladder when free from the anchoring effect of the stone. When, at cystoscopy, a stone is seen to be suspended from the wall of the bladder, it is safer to open the bladder to avoid the risk of grasping the wall in the lithotrite in attempting to grip the stone. Through the open wound the vesical mucosa may be examined for further sutures which may be on their way through the wall of the bladder.

[*Editorial Note*—The fact that foreign bodies passed into the urethra are swallowed or are left behind at abdominal operations and find their way to the bladder even as often as White's report would indicate, is of more than passing interest. The association of trauma and injury to the bladder and the encrustation of suture material is familiar to all. White's caution as to the use of the lithotrite in crushing the encrustations of foreign bodies is timely. Often much trauma may be necessary in disengaging the jaws of the lithotrite, and the cystostomy which the surgeon has tried to avoid will have to be performed under less favorable conditions than if it had been the initial procedure.]

#### PROSTATE GLAND

*Hypertrophy*—Weiser<sup>22</sup> stated that the most common changes encountered in cases of adenoma of the prostate gland are infection, malignant degeneration and poor results following prostatectomy. Tuberculosis of the male genital tract, which is usually of hematogenous origin, is not uncommon, and it is not impossible to find tubercles in a hypertrophied gland. Tuberculosis of the epididymis and seminal vesicles is of significance in this relation. Examination of clinical material in Weiser's hospital disclosed eighty-seven cases of genital tuberculosis, in only one of which the prostate gland alone was involved. Genital tuberculosis is a disease of youth and adenoma of old age.

A case was cited of a patient aged 72 who had urinary retention. Examination showed normal external genitalia and a large prostate gland of boggy consistence. The urine contained traces of albumin, leukocytes, epithelial cells and various types of cocci. Prostatectomy

<sup>22</sup> Weiser, A. Tuberkulose Infektion der hypertrophierten Prostata, *Ztschr f urol Chir* 28 105, 1929

was performed. The postoperative convalescence was slow. There was much coughing and expectoration but bacilli of tuberculosis were never found. The suprapubic fistula was open at the end of five months. The slow recovery of the patient was explained by finding an old cavernous tuberculous process, with contiguous new miliary processes, in one lobe of an adenomatous, hypertrophied prostate gland.

*Carcinoma*—Smith and Pearson<sup>23</sup> stated that the value of treatment for carcinoma of the prostate gland by high voltage roentgen rays has not yet been firmly established. From a study of twenty-five cases of carcinoma of the prostate gland treated by high voltage roentgen rays, they concluded that pain due to obstruction and to cystitis is not affected by irradiation and must be treated by appropriate measures. The roentgen rays will relieve other types of pain due to prostatic carcinoma and metastasis in most instances. The duration of relief is variable but usually lasts from one to six months after each series of treatments. In some cases the malignancy of the growth appears to be reduced, as evidenced by improvement in the patient's general condition and in the slowing up of the progress of the growth. Not more than three or four series of treatments at intervals of from two to three months, should be given.

*Tuberculosis*—Lowsley and Duff<sup>24</sup> stated that tuberculosis of the prostate gland is a frequent accompaniment of genital tuberculosis, but that it does not occur so often in urinary tuberculosis. Of the genito-urinary organs, the epididymis is most often affected by this disease, the kidney is next in frequency and is followed closely by the ureters and bladder. The seminal vesicles are occasionally the site of tuberculosis, usually after tuberculous epididymitis of long standing, and the prostate gland is least often affected. Primary tuberculosis of the gland is extremely rare. Tuberculosis of the genito-urinary tract is found at necropsy in a little more than 2 per cent of cases of pulmonary tuberculosis. In 70 per cent of the cases of urogenital tuberculosis there is coincident tuberculosis of the prostate gland, and in a small fraction of 1 per cent, primary tuberculosis of the gland.

The diagnosis of tuberculosis of the prostate gland is difficult, especially if it occurs in conjunction with benign adenomatous hypertrophy or if hard nodules are discovered on digital examination when the patient is of cancer age. If it is remembered that in all cases of urogenital tuberculosis the prostate gland is involved in 70 per cent, earlier diagnoses can be made and the chance for cure or of proportionate lengthening of life is increased.

<sup>23</sup> Smith, G. G., and Pearson, E. L. The Value of High Voltage X-Ray Therapy in Carcinoma of the Prostate, *J. Urol.* **23** 331 (March) 1930.

<sup>24</sup> Lowsley, O. S., and Duff, John. Tuberculosis of the Prostate Gland, *Ann. Surg.* **91** 106 (Jan.) 1930.



Surgical procedures are not ordinarily indicated in cases of tuberculosis of the prostate gland. In most cases in which the tuberculous gland has been removed, it was removed because of a mistake in diagnosis. It is Lowsley's practice to subject all patients to a continual period of observation and care. Some are given treatment by alpine light or by quartz light and others are given Koch's old tuberculin in graduated doses. Lowsley and Duff have used tuberculin for more than three years, not alone but as an adjunct or subsidiary agent in a regimen of treatment consisting of hygienic and dietetic measures, rest, mercury vapor, quartz light, heliotherapy and the urologic measures indicated. The general plan is to combine the urologic treatment with the tuberculous treatment to the extent it is applicable and adaptable to the needs of the individual patient.

Twenty-one of Lowsley and Duff's patients with tuberculosis of the prostate gland were operated on, only two operations were on the prostate gland. One of the two patients died a few weeks after leaving the hospital. Another patient improved under palliative treatment. Eight of the patients were given tuberculin and apparently were benefited. None of the patients was harmed by the tuberculin.

*(To be Continued)*

# ARCHIVES OF SURGERY

VOLUME 21 DECEMBER, 1930—IN TWO PARTS—PART I NUMBER 6

## TRIBROMETHANOL ANESTHESIA \*

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Of the anesthetic agents recently introduced into clinical practice, tribromethanol appears to be one of the most promising. The drug was first introduced in Germany nearly three years ago, and there are now from 300,000 to 400,000 cases in which it has been used. In spite of this fairly wide experience with it in Europe, there is still a great difference of opinion among clinicians regarding its usefulness. Because of this situation, we have attempted to gather together the available pharmacologic and clinical data, to verify a few points by experimentation on animals and, with the knowledge so obtained, to apply the anesthetic to the human being.

### REVIEW OF THE LITERATURE

#### CHEMICAL AND PHYSICAL PROPERTIES

Tribromethanol was first prepared, in 1923, by Willstatter and Duisberg<sup>1</sup> through the reduction of bromal hydrate in yeast-sugar fermentation. In the manufacture of the substance on a commercial scale, this method of preparation apparently has been replaced by a purely chemical synthesis. The latter process is based on the reduction of bromal hydrate by alcohol in the presence of aluminum ethoxide as a catalyst.<sup>2</sup> The pure drug consists of colorless monoclinic prisms, which are odorless and which melt at 80 C. According to Eichholtz,<sup>3</sup> it dissolves without decomposition in water heated to 45 C, but in water heated to about 70 C, the dissolved drug slowly hydrolyzes with the formation of hydrobromic acid and dibromacetaldehyde. On steam distillation of a solution of it, it is readily volatile. The solution of the pure drug in distilled water is neutral to congo red, but if heated to the point of hydrolysis, it becomes distinctly acid to this indicator. It is therefore recommended that solutions of the anesthetic be made

\* Submitted for publication, March 17, 1930.

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1 Willstatter, R, and Duisberg, W. Zur Kenntnis des Trichlor- und Tribromathyl-Alkohols, Ber d deutsch chem Gesellsch 56 2283, 1923.

2 British patent no 235,584, June 12, 1924.

3 Eichholtz, F. Ueber rektale Narkose mit Avertin (E 107) Pharmakologischer Teil, Deutsche med Wchnschr 53 710, 1927.

at a temperature not in excess of 45 C, and that they be tested with 0.1 per cent solution of congo red prior to instillation into the rectum, in order to avoid intestinal irritation resulting from the acid products of hydrolysis. When an aqueous solution of tribromethanol is permitted to stand for several days at room temperature, some decomposition takes place. For this reason, it has been recommended that solutions for rectal anesthesia be prepared less than twelve hours before use. Blomfield and Shipway<sup>4</sup> showed that 3 per cent solutions kept in the dark at room temperature remain neutral to congo red for about forty-eight hours. They quote other English workers who found no decomposition in a 3 per cent solution kept at room temperature for fourteen days, while Parsons<sup>5</sup> claimed to have kept solutions exposed to light and air for as long as three months without evidence of decomposition. Blomfield and Shipway observed that exposure of the solution to ultraviolet light produced rapid hydrolysis. The drug dissolves readily in alcohol, ether, ethyl acetate, chloroform, acetone, petroleic ether and similar organic solvents. It may be distilled in a high vacuum without decomposition, its boiling point at 11 mm pressure is 93 C.<sup>1</sup>

#### PHARMACOLOGIC ACTION

*Dosage*—Experiments by Eichholtz<sup>3</sup> indicate that the response of different species of animals used in ordinary laboratory experimentation varies over a considerable range. Thus, in cats, anesthesia is obtained following the oral administration of 0.15 Gm per kilogram of weight. Mice and rabbits, on the other hand, require oral doses as high as from 0.5 to 1.6 Gm per kilogram of body weight in order that anesthesia may be produced. Administration by rectum produces similar variations. Mice require only from 0.08 to 0.15 Gm per kilogram for the production of deep anesthesia, whereas dogs require 0.15 Gm per kilogram. When administered by rectal injection, the minimum lethal dose for experimental animals is from 75 to 100 per cent in excess of the anesthetic dose. Eichholtz tested the possibility of chronic poisoning from repeated injection of the drug by giving daily rectal doses of from 0.4 to 0.5 Gm per kilogram to white mice over a period of seven weeks. No tolerance to the drug was observed, and a pathologic examination of the tissues of these animals revealed no lesions. Induction of anesthesia in animals following rectal administration is rapid, the rate of recovery of rabbits from such anesthesia is said to be twice as rapid as that from chloroform.

<sup>4</sup> Blomfield, J, and Shipway, F. E. The Use of Avertin for Anesthesia, *Lancet* 1:546, 1929.

<sup>5</sup> Parsons, F. B. Some Pharmacological Aspects of Avertin, *Brit. M. J.* 2:709, 1929.

anesthesia and as fast as recovery from ether. Lendle<sup>6</sup> found that fasting animals were more susceptible to the effect of the anesthetic.

*Absorption*—Straub<sup>7</sup> studied the rate of absorption of the drug from the intestinal tract in three human beings in whom tribromethanol was used as a rectal anesthetic. They were persons of varying susceptibility to the drug and were studied in order to determine whether or not resistance to or susceptibility to the drug was reflected in the rate of its absorption from the intestine. His results indicated that so far as rate of absorption is concerned, there is no difference between the susceptible and the resistant subject. The drug was shown to have been almost quantitatively absorbed within a period of two hours following its administration.

Sebening<sup>8</sup> showed that the concentration of the drug in the blood stream rises to a maximum of 9 mg per hundred cubic centimeters twenty minutes after the rectal administration of the anesthetic solution. This concentration falls rapidly to 3 mg per hundred cubic centimeters, and then slowly to 0.15 mg per hundred cubic centimeters, a concentration at which awakening takes place.

That the rate of absorption of the drug from the intestine varies considerably during an anesthesia of two and one-half hours' duration is demonstrated by one of Straub's experiments. This showed that during the first seventeen minutes following rectal administration of the drug in 3 per cent solution, the tribromethanol was absorbed at the rate of 0.47 Gm per minute, and water was absorbed at the rate of 14.6 Gm per minute. Three further rectal injections of the drug made at subsequent intervals of from approximately one-half to one hour indicated that the rate of absorption of the drug through the intestinal wall had fallen to a value of from 0.04 to 0.08 Gm per minute, while the rate of absorption of water had fallen to a value of from 1 to 2 Gm per minute. This experiment shows clearly that the permeability of the intestinal wall decreases following the first rectal injection of tribromethanol.

*Excretion*—Endoh<sup>9</sup> demonstrated that tribromethanol is excreted in the urine of dogs and rabbits in conjugation with glycuronic acid. This was confirmed by Straub<sup>10</sup> in his study of the excretion of the

6 Lendle, L. Experimentelle Untersuchungen über die Dosierung und die Elimination des Avertins, Narkose u. Anaesth. **1** 239, 1928.

7 Straub, W. Rektalnarkose mit Avertin (Resorption und Dosierung), München med. Wchnschr. **75** 593, 1928.

8 Sebening, W. Report of 52nd Annual Meeting of German Surgeon Society, Berlin, April 11-14, 1928, Zentralbl. f. Chir. **55** 1360, 1928.

9 Endoh, C. Ueber das Verhalten des Tribromathyl-Alkohols im Tierkörper. Biochem. Ztschr. **152** 276, 1924.

10 Straub, W. Rektalnarkose mit Avertin. II. Ausscheidung und Nebenwirkungen, München med. Wchnschr. **75** 1279, 1928.

surgical anesthesia requires 64 per cent of the fatal dose. This is in line with experience with other general anesthetic agents, the dose of which for surgical anesthesia is believed to represent approximately from two-thirds to three-fourths the fatal amount.

*Effect on Blood Chemistry*—A study of the acid-base equilibrium during anesthesia from tribromethanol by Wymer and Fuss<sup>23</sup> showed that this drug more closely resembles chloroform than ether in its tendency to produce acidosis in experimental animals. During anesthesia in the human being, the hydrogen ion concentration of the blood was found to remain practically normal. The blood sugar rose sharply, but returned to the normal range in from six to twenty-four hours after the induction of the anesthesia. The alkali reserve was not materially altered.

Experiments by Stiasny<sup>24</sup> showed that the calcium content of the blood serum is decreased from 7 to 13 per cent during anesthesia produced by tribromethanol. In this respect, tribromethanol is similar to ether.

#### CLINICAL APPLICATION

Since tribromethanol has been used by numerous European clinicians in obtaining general anesthesia in cases numbering to hundreds of thousands, it is difficult to make a complete résumé of all the various techniques employed. The excellent review of Killian,<sup>25</sup> the reports of Anschutz<sup>26</sup> and of Blomfield and Shipway,<sup>4</sup> the two questionnaires of Schwalbe<sup>27</sup> and the symposiums of the German surgical societies provide a simple method for obtaining a fair approximation of previous experience with this new type of rectal anesthesia. A more recent report by Guttman<sup>28</sup> gives a résumé of the recent experiences of German workers. For detailed data, the original literature must be consulted.

23 Wymer, I, and Fuss, H. Die Saurebasenverhältnisse bei der Avertinnarkose, zugleich ein Beitrag zur pathologischen Physiologie der Avertinnarkose, *Deutsche Ztschr f Chir* **211** 281, 1928, Eine vergleichende Studie über die Saurebasenverhältnisse bei der Ather-Chloroform und Avertinnarkose, *Narkose u Anaesth* **1** 283, 1928.

24 Stiasny, H. Ueber Narkose mit Avertin (E-107) und ihren Einfluss auf den Serumkalziumspiegel beim Hunde, *Tierarztl Rundschau* **33** 871, 1927.

25 Killian, H. Die bisherigen Ergebnisse mit der Avertinrektalnarkose, *Narkose u Anaesth* **1** 16, 1928, Avertin-Rectal Anesthesia. The Results to Date, *Brit J Anesth* **5** 168, 1928, **6** 48, 1928.

26 Anschutz, W. Zur Eröffnung einer allgemeinen Aussprache über die Avertinnarkose, *Zentralbl f Chir* **55** 2371, 1928.

27 Schwalbe, J. Der gegenwartige Stand der Avertinnarkose. Eine Umfrage, *Deutsche med Wchnschr* **53** 2064, 1927, Ueber die Avertinnarkose. 2 Umfrage, *ibid* **54** 558, 1928.

28 Guttman, J. R. Rectal Anesthesia with Tribromethanol, *Ann Surg* **90** 407, 1929.

*Pneanesthetic Medication*—The general plan of the pneanesthetic technic employed by most of the German workers is uniform. The intestinal tract is emptied by an enema or mild cathartic the evening before the operation, and the patient is placed on a liquid diet. Barbitol is also given the evening before. The morning of the operation a hypodermic injection of pantopon, morphine, scopolamine or narcophine is given about one and one-half hours prior to the administration of tribromethanol. There is a wide variation of opinion regarding the advisability of giving such pneanesthetic narcotics. Although Kreuter<sup>29</sup> reported better anesthesia without these narcotics, the majority of the clinicians use one or more of these drugs, administered by hypodermic injection.

*Preparation of Solution*—Tribromethanol is usually administered in 3 per cent solution in distilled water at body temperature. In order to hasten solution, the crystalline drug is dissolved in warm water at temperatures not to exceed 45 C. A few clinicians recommend temperatures not in excess of 60 C. Because of hydrolysis, solutions are not used more than twelve hours after their preparation. It is customary to test the solution with congo red just prior to its administration. Any solution giving an acid reaction must be discarded.

Although most surgical clinics use tribromethanol in 3 per cent solution, a few have found it advisable to work with lower concentrations. Glaesmer and Amersbach<sup>30</sup> varied the concentration of the drug between the limits of 2 per cent and 3 per cent depending on the age of the patient. In aged patients, low concentrations and low dosages are employed, whereas in youthful patients a higher concentration is utilized. Martin<sup>19</sup> reported good results with 2.5 per cent solution of the drug, but no advantage appears to obtain from the employment of the more dilute solution.<sup>31</sup>

In place of distilled water, some workers<sup>32</sup> recommended physiologic solution of sodium chloride as a solvent for the drug. Nordmann<sup>33</sup> seemed to have difficulty with intestinal irritation following the use of aqueous solutions. The use of 1 per cent salep mucilage as a solvent was found to obviate this difficulty. Other workers use milk as a solvent.

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29 Kreuter, E. Sechshundertfünfzig Rektalnarkosen mit Avertin (E 107), Zentralbl f Chir **54** 3074, 1927.

30 Glaesmer, E., and Amersbach, R. Zur Kritik der Avertinnarkose, München med Wchnschr **74** 1835, 1927.

31 Butzengeiger, O. Zur Avertin Aussprache, Zentralbl f Chir **56** 204, 1929.

32 Melzner, E. Zur Beurteilung der Rectalnarkose mit E 107 (Avertin), Arch f klin Chir **148** 698, 1927. Lobenhoffer, W. Ueber Narkosen mit E 107, München med Wchnschr **74** 849, 1927.

33 Nordmann, O. Die Rektalnarkose mit E 107, Zentralbl f Chir **54** 1055, 1927.

The majority of German clinicians report little difficulty from intestinal irritation when neutral aqueous solutions are used

A recent modification by Schulze<sup>34</sup> is the use of a solution of tribromethanol in amylene hydrate (tertiary amyl alcohol). A solution may be obtained, 1 cc of which will contain 1 Gm of tribromethanol and 0.5 Gm of amylene hydrate. Apparently this solution is comparatively stable. Amylene hydrate is said to be not only a good solvent for the drug, but the ease of volumetric measurement of such a solution avoids the necessity of weighing out the drug. One may simply measure out the requisite dose of drug with a pipet and add the necessary amount of water at body temperature. Amylene hydrate exerts a mild narcotic effect of its own, and is said to have a stimulating effect on the respiratory center which partially offsets the depressing effect of the tribromethanol.

*Dosage*—The dosage of tribromethanol employed by German workers in producing general anesthesia has varied from 0.08 Gm per kilogram to over 0.2 Gm per kilogram. The first American workers to report on the use of tribromethanol as a rectally administered anesthetic were Honan and Spiegel<sup>35</sup>. They recommended dosages of from 0.1 to 0.15 Gm per kilogram of body weight, although in the cases that they reported the patients were all treated with from 0.15 to 0.175 Gm per kilogram of body weight. Few clinicians exceed 0.15 Gm per kilogram, and the general trend seems to be toward a dosage of 0.125 Gm per kilogram or less. Most of the deaths reported during tribromethanol anesthesia have followed the administration of doses of 0.15 Gm or more per kilogram of body weight. According to Nordmann,<sup>36</sup> the dose recommended by the manufacturer of the drug is 0.1 Gm per kilogram. Koller<sup>36</sup> came to the conclusion that 0.15 Gm per kilogram is too high a dose in a case of pulmonary involvement. Butzengeiger<sup>37</sup> used a scheme of fractional dosage that appears to have worked out satisfactorily. The method is to give a basal dose of 0.1 Gm per kilogram. If sleep has not supervened in from five to seven minutes, a further injection of 0.025 Gm per kilogram is given. If this still fails to produce surgical anesthesia in another ten or fifteen minutes, a final injection of 0.025 Gm per kilogram is given. This makes a total of 0.15 Gm per kilogram, which he does not recommend exceeding. If necessary, deeper anesthesia is obtained by

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34 Schulze, W. Ueber Rektalnarkosen mit Avertin-Amylenhydratlösung, *Deutsche med. Wchnschr.* **54** 1928, 1928.

35 Honan, W. F., and Spiegel, A. Colonic Anesthesia with Avertin, *J. A. Inst. Homœop.* **22** 7, 1929.

36 Koller, T. Avertinnarkose bei Phrenicusexstirpation, *Zentralbl. f. Chir.* **55** 2498, 1928.

37 Butzengeiger, O. Klinische Erfahrungen mit Avertin (E 107), *Deutsche med. Wchnschr.* **53** 712, 1927, footnote 31.

supplementary inhalation of ether. Schulze<sup>34</sup> uses a similar method, but employs 0.125 Gm per kilogram as the usual basal dose for adults, and 0.15 Gm per kilogram for children. In either case, only one additional injection of 0.025 Gm per kilogram is made, if the desired grade of anesthesia is not obtained.

The obvious trend of European technique in producing anesthesia with tribromethanol is toward a more conservative scheme of dosage. This is accomplished by administering a basal dose followed by a succeeding dose if needed, or by supplementing the basal tribromethanol anesthesia by means of inhalation or local anesthesia. The latter method is advocated by the English clinicians.<sup>4</sup>

*Depth and Duration of Anesthesia*—The depth and duration of the anesthesia following rectal administration of tribromethanol vary widely in different persons. Although Roith<sup>38</sup> was unable to observe any variation of susceptibility in patients of different ages, most workers report a decreased response of children to the anesthetic. Schulze<sup>34</sup> found that while only 30 per cent of children (from 1 to 10 years of age) were completely anesthetized by the drug, from 55 per cent to 75 per cent of older subjects (from 10 to 70 years of age) were completely anesthetized by a similar dose. Statistics given by Roith,<sup>38</sup> Kreuter,<sup>39</sup> Conrad<sup>39</sup> and Lobenhoffer<sup>40</sup> indicate that at single doses of from 0.12 to 0.15 Gm per kilogram, about 60 per cent of all patients give complete surgical anesthesia. In from 15 per cent to 30 per cent, a small amount of accessory anesthetic (ether, ethyl chloride, acetylene, ethylene or methylene chloride, but not chloroform) was required for securing the necessary depth of narcosis. A similar percentage required a moderate amount of accessory anesthetic, but only from 3 to 10 per cent required considerable quantities of additional anesthetic.

According to European clinicians, blood pressure under tribromethanol anesthesia usually either remains unchanged or falls slightly (from 10 to 30 mm mercury). Respiration is not greatly affected. The pupils are constricted. A characteristic flushing of the face has been noted. The body temperature falls slightly. Cyanosis is said to be comparatively rare.

In the European clinics, administration of the solution is accomplished by means of a small rubber catheter and syringe. The catheter is usually inserted into the rectum to a depth not in excess of 20 cm. Lobenhoffer<sup>40</sup> devised a rectal tube fitted with a rubber balloon, which is separately inflated so as to prevent leakage of the anesthetic solution.

38 Roith, O. Zur Avertinnarkose, München med Wchnschr. **75** 598, 1928.

39 Conrad, G. Klinische Erfahrungen über die Rektalnarkose mit Avertin (E 107) bei gynäkologischen und geburtshilflichen Operationen, Zentralbl f Gynak. **51** 2222, 1927.

40 Lobenhoffer (footnote 32, second reference).



According to the German clinicians, one of the most desirable features about tribromethanol anesthesia is the ease of its induction and of recovery from it and the comparative freedom from nausea and vomiting. Following the administration of the anesthetic, the patient becomes more and more drowsy and in about seven minutes has fallen into a deep sleep. In from fifteen to twenty minutes, anesthesia has reached the depth required for operation. The duration of deep anesthesia varies considerably over a range of from one to six hours, depending on the person and the dose. This is followed by gradual awakening. There is no period of excitement during either the induction or the recovery. Nausea and vomiting are said to be extremely rare, except in cases in which considerable ether has been used as an additional anesthetic. The patient has no recollection of anything that has taken place during the latter period of the induction or during the operative procedure. Levy-Dorn<sup>41</sup> considered these desirable aspects of tribromethanol anesthesia to be of great importance in the justification of its clinical use.

*Dangers and Remedies*—The chief dangers encountered in the use of tribromethanol for the production of anesthesia (aside from the use of overheated, hydrolyzed solutions and overdosage) appear to be incidental to excessive depression of the respiration and circulatory mechanism and impairment of the secretory organs through which the drug is detoxified. Embarrassment of respiration and heart was successfully handled by Melzner<sup>42</sup> by the intravenous injection of caffeine and epinephrine or by washing out the intestine with a caffeine solution. The antidotal action of caffeine injected intravenously was demonstrated in animals by Herzberg<sup>43</sup>. Such injections were found to have a marked effect in shortening the duration of narcosis, as well as in decreasing its depth. He was unable to protect animals against the ordinarily fatal dose of tribromethanol by means of the injection of caffeine, however. There apparently is a difference of opinion as to the value of ephedrine in combating circulatory depression during tribromethanol anesthesia. Schmidt<sup>43</sup> reported beneficial effects and recommended it as a prophylactic agent, while Schrank<sup>44</sup> found it to be of no value. As has been pointed out earlier in this discussion, several clinicians found carbon

41 Levy-Dorn M. Vergleich zwischen Aether- und Rektal-narkose mit E 107 (Avertin), *Med. Klin.* **23** 871, 1927.

42 Herzberg, M. H. Pharmakologische Versuche mit Avertin, *Deutsche med. Wchnschr.* **54** 1044, 1928.

43 Schmidt, H. Das Ephedrin in der operativen Praxis, *Zentralbl. f. Chir.* **55** 3207, 1928.

44 Schrank, H. Avertin und Kreislauf, *Zentralbl. f. Chir.* **55** 3205, 1928.

dioxide to be of no value in stimulating respiration during the anesthesia. The efficacy of lobeline as a respiratory stimulant does not seem to have been satisfactorily established. Tribromethanol for the production of anesthesia is said to be contraindicated in cases of damaged kidneys and liver, serious hypertension and cachexia. In addition to its use in general surgery, the anesthetic has found application in psychiatry in the handling of excited patients<sup>45</sup>. Its use in childbirth does not seem to have met with such great success<sup>46</sup>. Lawen<sup>47</sup> found it to be of value in the treatment for tetanus.

Deaths that are fairly attributable to reasonably conservative doses of tribromethanol are comparatively rare. Glaesmer and Amersbach<sup>40</sup> cited records of 13 deaths in 3,000 anesthetics. They further analyzed these 13 fatal instances and showed that, in general, the deaths were in connection with the use of hydrolyzed anesthetic solution, overdosage or a poor grade of surgical risk. Similar estimates of the mortality from the use of tribromethanol for the production of anesthesia have been made by Kotzoglú<sup>48</sup> and by König<sup>49</sup>. A later estimate of the mortality in tribromethanol anesthesia is 1 in 7,500<sup>50</sup>.

#### PHARMACOLOGIC STUDIES OF TRIBROMETHANOL

The first preparation of tribromethanol used was supplied by Dr. Helmut Schmidt of the Hamburg-Eppendorf Hospital, Germany. A further supply was provided by the Winthrop Chemical Company. It was a white, crystalline powder melting sharply at from 79.5 to 80°C. Chemical analysis by the Carus method showed the product to contain 84.9 per cent bromine, which corresponds favorably with the theoretical value of 84.8 per cent for tribromethanol.

45 Blume, G. Ueber Avertin in der Psychiatrie, *Deutsche med. Wchnschr.* **53** 1307, 1927. Enke, W., and Westphal, K. Avertin als Hypnotikum und Dauerschlafmittel in der Psychiatrie, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **114** 616, 1928.

46 Martin, E. Avertin in der Geburtshilfe, *Monatschr. f. Geburtsh. u. Gynäk.* **76** 241, 1927. Rodecourt, M. Ueber Avertinnarkose bei gynäkologischen Operationen, *Narkose u. Anaesth.* **2** 39, 1929. Ujma, A. Die Rektalnarkose bei gynäkologischen Operationen, *Narkose u. Anaesth.* **1** 329, 1928. Mey, R. Avertindammerschlaf, *Zentralbl. f. Gynäk.* **52** 1127, 1928. Kienlin, H. Bestrebungen zum Ausbau des geburtshilflichen Dammerschlafes, *Zentralbl. f. Gynäk.* **52** 1946, 1928.

47 Lawen, A. Weitere Erfahrungen über die symptomatische Behandlung des Tetanus mit Avertin, *Zentralbl. f. Chir.* **55** 194, 1928.

48 Kotzoglú, P. Ueber die Todesfälle in Avertinnarkose, *Zentralbl. f. Chir.* **56** 2206, 1929.

49 König. *Zentralbl. f. Chir.* **56** 1895, 1929.

50 Proceedings of the Northwest German Surgical Society, Dec. 14-15, 1928 (Avertin Aussprache), *Zentralbl. f. Chir.* **56** 995, 1929.

## PRELIMINARY ESTIMATIONS

*Solubility*—Solutions of known concentration from 0.5 to 3 per cent of tribromethanol in distilled water were prepared and their refractive indexes determined at 40 C by means of the immersion refractometer. From these data, the concentration of any solution in the range from 0 to 3.5 per cent tribromethanol could be calculated from its refractive index. Saturated solutions of tribromethanol in distilled water were prepared at room temperatures varying from 0 to 37 C, and the refractive indexes of such saturated solutions were determined at 40 C. The solubility of tribromethanol in this range of temperature is indicated in table 1. From table 1, it would be expected that a 3 per cent solution would deposit crystals of tribromethanol when cooling below 25 C.

TABLE 1—*The Solubility of Tribromethanol at Temperatures from 0 to 37 C*

Temperature, C	Grams Tribromethanol per 100 Cc. Solution
0	1.90
9	2.15
26	3.05
37	3.70

TABLE 2—*Results of Intraperitoneal Injection of Tribromethanol\* in Rats*

Dosage, Gm. per Kg.	Results
0.50	Three animals died in fifteen minutes
0.45	Of three animals, two died within fifteen minutes
0.40	Of five animals, one died within fifteen minutes
0.35	Of eleven animals, one died in fifteen minutes, surgical anesthesia lasted from twenty to forty minutes
0.30	Light anesthesia lasted for from twenty to thirty minutes
0.20	Sleep lasted for nine minutes

\* Three per cent aqueous solution of the crystals

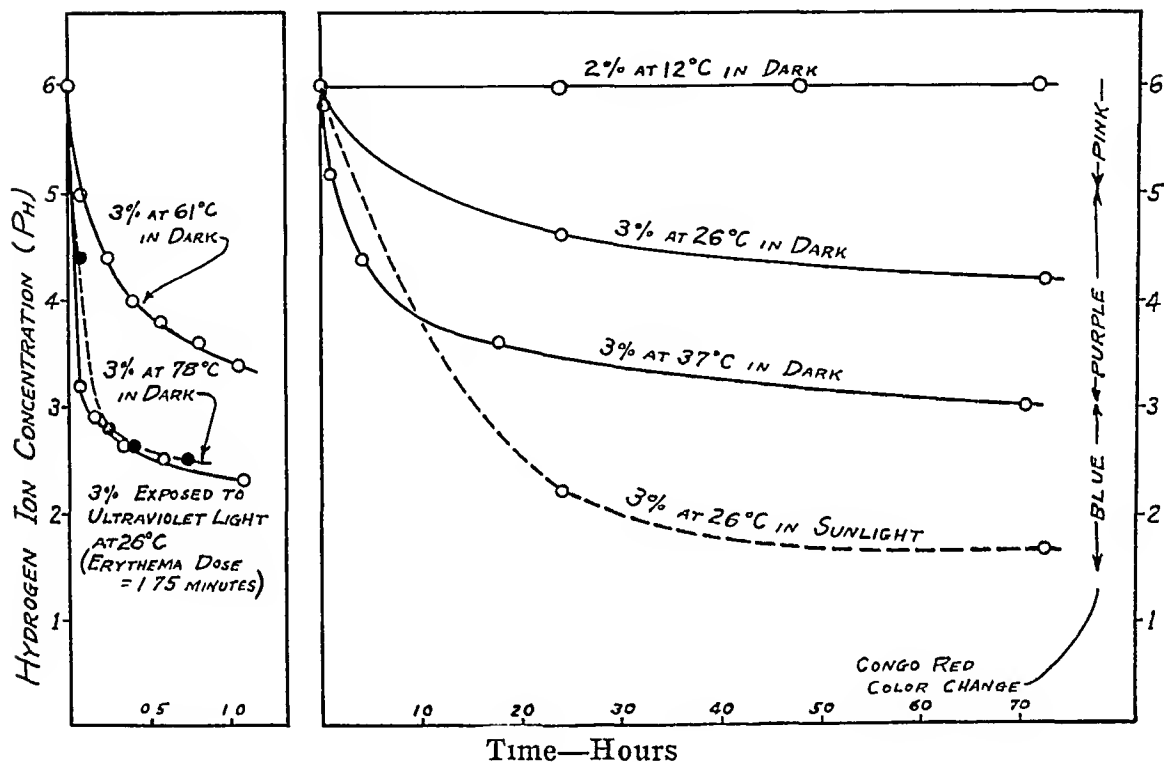
*Stability toward Hydrolysis*—A study of the changes in the hydrogen ion concentration of tribromethanol solutions under varying conditions was made. The original solutions were prepared in the usual way by dissolving crystals of tribromethanol in ordinary distilled water at 40 C. Such solutions had the same hydrogen ion concentration as the water (from 5.8 to 6). The hydrogen ion concentration was determined by the colorimetric method, the indicator series of Clarke being used. The results are indicated in the accompanying chart.

## TOXICITY AND EFFICIENCY IN EXPERIMENTAL ANIMALS

*Rats*—Intraperitoneal injections of tribromethanol (3 per cent aqueous solution of the crystals) produced results as set forth in table 2. Rats given daily intraperitoneal doses of 0.3 Gm. per kilogram of body weight over a period of a week showed no evidence of cumulative action.

Tribromethanol in the soluble form (66 per cent by weight of tribromethanol and 34 per cent of tertiary amyl alcohol) was found to be slightly more toxic to rats than the crystalline form of the drug. The amyl alcohol apparently adds slightly to the toxicity of the preparation, since the average fatal dose was reduced from 0.45 to 0.37 Gm per kilogram of body weight.

*Rabbits*—The maximum oral dose which may safely be administered to rabbits is about 0.8 Gm per kilogram of body weight (given in 3 per cent aqueous solution). This gives an anesthesia lasting from about



Changes in the hydrogen ion concentration of solutions of tribromethanol under various conditions

twenty to forty minutes. A moderately deep anesthesia, lasting from nine to twenty-four minutes, is obtained with 0.7 Gm per kilogram, given orally. Lower doses produce sleep, but no anesthesia.

Intravenous doses of 3 per cent aqueous solution of tribromethanol produced a sudden but brief anesthesia. A slowly injected dose of 0.2 Gm per kilogram of body weight was about the maximum that was tolerated. This produced anesthesia for approximately fifteen minutes. A dose of 0.15 Gm per kilogram gave surgical anesthesia for only a few minutes, followed by a deep sleep of about ten minutes. Doses of 0.10 Gm per kilogram produced only a deep sleep.

In order to ascertain the effect of tribromethanol on erythrocytes, rabbits' blood was added to solutions of the drug made up in physiologic solution of sodium chloride. At 37 C complete hemolysis was observed within fifteen minutes in concentrations of 1.5 per cent and 2 per cent tribromethanol. One per cent solution produced partial hemolysis. Blood taken from rabbits that had received intravenous injections of 0.2 Gm of tribromethanol per kilogram gave no evidence of hemolysis on centrifugation. Animals so anesthetized did not develop a hemoglobinuria. Any extensive hemolysis due to the low concentration of the injected drug seems improbable. Application of a 3 per cent aqueous solution of crystals of tribromethanol to the rabbit's cornea produced no apparent painful sensation, but gave rise to an anesthesia that was maintained for approximately twenty minutes. That slight irritation was produced was evidenced by the resulting congestion of the blood vessels of the eye. A 3 per cent solution of tribromethanol prepared from the fluid (67 per cent tribromethanol + 33 per cent amylene hydrate), when instilled into the conjunctival sac of a rabbit, produced somewhat greater congestion than the solution prepared from the crystalline form of the drug. No permanent harmful effects were observed.

*Protection Against Toxic Effects of Cocaine and Procaine*—Since tribromethanol has been recommended as a basal narcotic for local anesthesia, particularly in ophthalmologic work, the question of its possible effect on the toxicity of local anesthetic agents was raised. Rabbits were given an ordinary anesthetic dose (oral), 0.7 Gm of tribromethanol per kilogram of body weight followed at once by a subcutaneous injection of cocaine hydrochloride. It was found that rabbits that ordinarily succumb to an injection of 100 mg of cocaine hydrochloride per kilogram will withstand 300 mg per kilogram under tribromethanol anesthesia. The ordinary fatal dose of procaine hydrochloride for rabbits is 800 mg per kilogram. Under tribromethanol anesthesia, rabbits survived doses of 1.2 Gm of procaine hydrochloride per kilogram. It is thus evident that tribromethanol anesthesia acts as a prophylactic agent against three times the ordinary fatal dose of cocaine hydrochloride, and 1.5 times the ordinary fatal dose of procaine hydrochloride.

*Dogs*—In accordance with the recommended technic for producing anesthesia in man by rectal injection of tribromethanol, in dogs the administration of the anesthetic was preceded by a subcutaneous dose of morphine sulphate. This consisted of a total dose of from 30 to 45 mg of morphine sulphate for each animal, administered about thirty minutes before the injection of tribromethanol. The tribromethanol was given in a freshly prepared 3 per cent aqueous solution, which was tested with congo red indicator to insure freedom from the acid products of hydrolysis. The dosage ranged from 0.3 to 0.5 Gm per kilogram.

of body weight. Surgical anesthesia developed within five minutes from the time of rectal administration and lasted for from fifteen minutes to one and one-half hours. It was noted that the more emaciated animals showed anesthesia of greater duration. Respiration was usually slowed but the pulse rate was not markedly altered. When no pre-anesthetic dose of morphine was given, doses of from 0.26 to 0.33 Gm. of tribromethanol per kilogram of body weight produced a deep sleep, but the duration of surgical anesthesia was never more than six minutes. The rectal temperature of the animals fell consistently during the anesthesia.

Three animals were given repeated rectal injections of from 0.3 to 0.4 Gm. of tribromethanol per kilogram of body weight, preceded by the usual dose of from 30 to 45 mg. of morphine sulphate. The anesthetic was given at intervals of from two to five days until each animal had received the anesthetic eight, fourteen and twenty times. Two of the three animals had pulmonary infection during the experiment, possibly brought on by unavoidable chilling during the anesthetics. One of the animals had pulmonary and renal tuberculosis. These tuberculous lesions have not been included in the pathologic description. No marked alteration in susceptibility to the anesthetic was noted. All animals, however, lost weight during the series of anesthetics. The animals were finally killed and examined post mortem. The observations at autopsy were as follows:<sup>51</sup>

The heart showed no gross changes. In histologic examination, it showed slight hydropic degeneration.

In one of the three animals, gross inspection of the lungs indicated pneumonia. Histologic examination showed acute bronchial pneumonia in this case and tuberculosis in another case. The lungs of one animal that had received twenty anesthetics were normal both grossly and microscopically.

On gross observation the liver presented possible fat. On histologic examination, the parenchyma showed marked swelling of the cells, which almost obliterated the capillary field. The individual cells were extremely pale and vacuolated, and showed coagulated, eosin-staining granules throughout. The vacuoles were evidently serous rather than fatty. In one case, most of the cells were distinctly atrophic.

Microscopic examination of the kidneys showed congestion of the glomeruli and parenchymatous degeneration of the tubules, with much albumin in the lumen. In two cases, there was some boundary zone necrosis with serous vacuoles in the living cells. In one case, there were localized areas of lymphatic polymorphonuclear infiltration of the interstitial tissue.

There was evidence of damage to the corpuscles of the spleen in all three cases, one showing necrosis, the other two hyperplasia. There was accumulation of hemosiderin in two cases.

The pancreas was normal.

In one case, acute ulcerative colitis was noted.

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<sup>51</sup> Prof. C. H. Bunting of the Department of Pathology of the University of Wisconsin made the pathologic studies.

Intravenous injection of 3 per cent solution of tribromethanol in physiologic solution of sodium chloride into dogs produced a sudden but brief anesthesia. Doses of from 0.06 to 0.12 Gm per kilogram of body weight produced surgical anesthesia of from seven to ten minutes' duration. Recovery was rapid.

A 3 per cent solution of tribromethanol in physiologic solution of sodium chloride was administered to several dogs without previous medication. From 2 to 4 cc per kilogram resulted in instantaneous anesthesia of durations varying with the dosage. Anesthesia was immediate and profound. Recovery was gradual compared with the induction, but rapid compared with the recovery following the use of any other method. For example, a dog weighing 9 Kg receiving no premedication was given 35 cc of 3 per cent solution of tribromethanol in physiologic solution of sodium chloride intravenously. Anesthesia was immediate and profound, with complete relaxation, lasting ten minutes. Gradual recovery took place, and eighteen minutes after injection the dog was on his feet and eating a dog biscuit with evident relish.

With the assistance of Prof. E. G. Hastings, of the department of agricultural bacteriology, the effect of tribromethanol on microorganisms was studied. In 3 per cent solution, the drug was found to have a definite bactericidal action.

#### CLINICAL INVESTIGATION OF TRIBROMETHANOL

In June, 1928, through Dr. Helmut Schmidt we were fortunate in having a clinical demonstration of tribromethanol and the technic of its administration. Following this demonstration, we began a laboratory and clinical investigation of the drug.

In view of the foregoing reports quoted from the literature and the data from the laboratories of pharmacology and experimental surgery of the University of Wisconsin Medical School, we felt that the exceptionally comfortable induction of surgical anesthesia by means of tribromethanol gave promise of filling a real need. Unreasonable and terror-stricken patients, particularly children, are difficult subjects for anesthesia and operation. The rectal administration of ether requires such a thorough preparation and necessitates such elaborate technic that a substitute seemed highly desirable.

The technic which we shall describe and which we have followed largely throughout our work with tribromethanol is based on the instructions originally given us by Schmidt, and elaborated somewhat as a result of our own personal experiences.

#### TECHNIC

*Ward Preparation of Patient*—Sufficient bland enemas (water or physiologic solution of sodium chloride) to empty the lower bowel completely are given as a

routine As a preanesthetic narcotic, we customarily use morphine and scopolamine, administered by hypodermic injection one and one-half hours before the expected time of administration of tribromethanol Doses are ordered that we should expect to be satisfactory were an anesthesia from gas-oxygen contemplated Premedication we believe to be desirable for a satisfactory anesthesia, furthermore, a careful observation of the effect of such premedication is a valuable guide as to the probable need for an increase or reduction of the calculated dose of tribromethanol Infants are given no premedication

*Preparation of Solution*—The hospital pharmacist delivers crystals to us weighed up in 3 Gm packets folded in paper, similar to the powders that he prepares for bedside administration of various drugs These 3 Gm powders combined with 100 cc of distilled water, or any multiple of these quantities, are brought into solution by agitation in a 500 cc Erlenmeyer flask held in a water bath kept at a temperature between 40 and 44 C, or from 104 to 110 F When complete solution is accomplished, a 5 cc sample is tested by the addition of from one to three drops of a 1:1,000 congo red solution If the red changes to purple or blue, the solution is discarded Fresh solutions are prepared daily

*Dosage*—A basic dose of 0.1 Gm of tribromethanol per kilogram or 15 cc of a 3 per cent solution per pound of the patient's body weight is usually used

*Instillation*—A 3 per cent solution properly prepared is apparently less unpleasant than distilled water in contact with the rectal mucosa This is probably due to the mild local anesthetic effect exerted by the drug

A soft rubber urethral catheter (no 10 French) is inserted into the rectum past the sphincter muscle Two strips of adhesive plaster are used to pull the buttocks firmly together around the catheter Adhesive strips are allowed to cross in the center and have contact with the catheter, thus holding it in place Care in fixing the catheter firmly in place saves much embarrassment in the prevention of the solutions leaking out after muscular relaxation has developed A 50 cc glass syringe is found convenient with which to measure and inject the solution, which should be at body temperature Extremely slow injection of the first 50 cc is preferable, because apparently the local anesthetic effect on the rectal mucosa obtunds the rectal reflex with tendency to expulsion of the solution

*Supplemental Anesthesia*—It seems to us highly desirable that the final accomplishment of complete surgical anesthesia be dependent on a drug under quick control The variations in tolerance of drugs by different persons is so great that an attempt to predetermine what dose will accomplish surgical anesthesia in a given person is dangerous We attempt, therefore, by means of tribromethanol, to deepen the sleep of a patient to a plane from which surgical anesthesia can be easily reached with a light dosage of nitrous oxide Whatever the inhalation agent used to complete anesthesia begun by tribromethanol, the dosage must be carefully regulated, and an abundance of oxygen and a free airway assured

It seems justifiable in some cases to prolong the effect of tribromethanol during an extremely long operation by further instillations of the drug during operation For the ordinary operation, lasting less than ninety minutes, additional quantities of tribromethanol may result in a deep anesthesia at the end of operation, accompanied by abolished reflexes, at a time when the patient must pass from the careful supervision of the anesthetist to that of the busy ward nurses In most instances, therefore, supplementation with nitrous oxide is recommended in preference to additional instillations of tribromethanol

*Supervision*—In no case does the anesthetist fail to follow his patient through the operation with the minute supervision which he would accord patients anesthetized by inhalation of anesthetic gases or vapors Pharyngeal airways are used



in most cases, and oxygen is added through them on many occasions. This practice is followed because we feel that oxygen is a factor of no small moment in the successful administration of other agents, and that a new drug deserves like consideration. In addition, it appears to us that many of the untoward results reported by others could be ascribed to effects secondary to respiratory obstruction and anoxemia. The excellent relaxation of pharyngeal muscles accompanying this form of anesthesia justifies such a conclusion.

Careful supervision during the period of anesthesia is just as necessary with this drug as with any drug administered by inhalation. Our one unfortunate experience occurred in a case in which complete deep anesthesia was attempted with tribromethanol alone. A child, 18 months old, weighing 24 pounds (10.9 Kg.), whose calculated dose was 36 cc. of a 3 per cent solution, was given a dose of 50 cc. Operation was begun ten minutes after instillation. The child was of the type subject to respiratory obstruction on the slightest provocation. The period of operation was characterized by difficulty in maintaining a clear airway, and anesthesia was still present when the operation was finished. The child was allowed to go back to the ward, without an artificial pharyngeal airway. Respiratory obstruction supervened three hours later, in the absence of sufficient supervision, and death resulted. The same accident would doubtless have occurred had the child been given ether in extreme dosage, and had the same faulty supervision existed. In no case should the patient be left without supervision before pharyngeal reflex and muscular tone have returned. Metal pharyngeal airways in place during operation and thereafter until no longer tolerated seem essential in tribromethanol anesthesia. The advantage of controlling the final depth of anesthesia with a labile agent, such as nitrous oxide, which can be adjusted at one's finger-tips, is evident. Under no circumstances should the supply of oxygen be deficient. An excess of oxygen and correction of a faulty airway often "smooth out" an anesthesia that appears to be insufficiently deep.

#### OBSERVATIONS

Tribromethanol has been used at the Wisconsin General Hospital in 234 clinical cases. Selection of these cases was made to cover as wide a range of risks as possible, as well as to cover a wide variety of surgical procedures. An analysis of the first 100 cases follows.

*Induction*—The absorption of the drug by the circulation following rectal instillation appeared to us to result in a normal "going to sleep." Children without previous opiates sometimes yawned and announced that they felt sleepy during the induction, but seldom complained of discomfort. Children who had already undergone the ordeal of the ward enema were happily relieved to find that this was so much easier. Unconsciousness usually came on within from three to five minutes from the beginning of instillation. Just as one child was going to sleep, she whispered the statement that she felt sick at her stomach. This was the nearest to evidence of nausea that we encountered during induction. In the total number of cases, we did not see vomiting occur during either induction or operation, in spite of the fact that in most of the cases anesthesia was administered for operations on the head, and in many it appeared to be light.

The pharyngeal reflex was abolished early, so that a rigid pharyngeal airway could usually be inserted long before operation was begun. Our impression is that the laryngeal reflex disappears only with excessive dosage. If this impression is borne out by more extensive experience, it is of the greatest value in anesthesia, since the activity of the "watch-dog of the lungs" is highly desirable during the period of unconsciousness. There was no tendency to an excessive secretion of mucus in the mouth and pharynx, even in the patients not receiving premedication. The skin reflex, or muscular reaction as the result of incision of the skin, disappeared late. This proved an embarrassment in cases of circumcision and perineorrhaphy.

Muscular relaxation suitable for laparotomy was often secured with the calculated dose mentioned. Our impression is that with increasing dosage of tribromethanol ascending paralysis of the spinal cord takes place, similar to that seen with increasing dosage of ether. We noted at least two cases in which there was partial intercostal paralysis. In both of these cases, the systolic blood pressure dropped during the respiratory depression. We see no advantage in an increase of the dosage of tribromethanol to accomplish complete anesthesia. We prefer to add a more labile agent that can be introduced and exhaled through the alveolar walls.

*Duration of Anesthesia, Recovery*—With the use of a solution of tribromethanol, prepared from crystals of tribromethanol, recoveries compared in length of time with those from anesthesia from ether.

*After-Effects*—No clinical evidence of proctitis or other irritation was noted in any case. Restlessness after the use of the solution prepared from crystals was not frequent or marked.

*Urinary Changes*—An attempted analysis of preoperative and postoperative urinary observations, as reported through routine laboratory analyses by hospital technicians, shows changes comparable to those found after operation in which other anesthetic agents have been employed. We do not believe these determinations to be of consistent value, but present them as we found them.

No case of suppression of urine was noted. Analysis of sixty-four urinary records gave the following figures. In twelve cases, the postoperative specimen of urine gave a positive result in the test for acetone, acetone not being noted in the preoperative specimen, in ten cases, casts were shown, in twelve, albumin. On the other hand, in nine cases the test for albumin gave negative results after operation, whereas there had been positive results before operation. No clinical evidence of damage to liver or kidneys came to our notice. The care with which respiratory obstruction and anoxemia were avoided may account for the absence of damage to liver or kidneys.

*Alterations of the Blood Chemistry*—Study was made in a few cases (fifteen) of some of the chemical constituents of the blood before and after anesthesia produced with tribromethanol, to ascertain whether any changes would be revealed as an immediate effect of the drug. For this purpose, blood was taken from the patient's vein just previous to rectal instillation, and again immediately following the completion of operation. The average length of time elapsing between the taking of the two samples was from an hour to an hour and a half. Determinations of nonprotein nitrogen, sugar, alkali reserve (carbon dioxide-combining power of plasma) and sodium chloride were made on each sample. From the results presented in table 3, it will be seen that no significant or consistent changes were noted. No information is at hand for judging the possibility of delayed changes.

TABLE 3—*Blood Chemistry in Anesthesia from Tribromethanol*

Case	Preanesthetic				Postanesthetic			
	Sugar, Mg	Nonprotein Nitrogen, Mg	Sodium Chloride, Mg	Alkali Reserve, Mg	Sugar, Mg	Nonprotein Nitrogen, Mg	Sodium Chloride, Mg	Alkali Reserve, Mg
1	96.0	33.9	479	29.4	111	34.7	462	43.7
2	103.0	40.7	432	36.5 (hemolyzed)	119	38.2	430	33.6 (slightly hemolyzed)
3	80.0	34.4	465	51.4 (hemolyzed)	110	29.0	447	
4	86.0	40.5	340	Sample short	105	37.4	316	36.0
5	80.5	22.6	449	52.1	144	22.3	465	35.4
6	61.5	33.6	432	27.2 (badly hemolyzed)	116	35.8	469	23.9
7	84.0	33.9	485	41.7 (slightly hemolyzed)	122	34.0	452	29.9

The rise in blood sugar is decidedly less than similar observation has revealed with various inhalation agents. Other changes are within the range of experimental error. The changes noted are in essential agreement with those reported by Wymer and Fuss<sup>23</sup>.

*Somatic vs. Psychic Effect*—The following case is described in detail because it illustrates the fact that apparently tribromethanol is primarily a somatic sedative and not a cerebral sedative. A knowledge of this fact is essential to a proper use of the drug.

A young man was seen suffering from acute manic-depressive psychosis, manic phase, of three weeks' duration. He could not be quieted by excessive doses of morphine, paraldehyde, chloral, etc. When given 0.1 Gm. of tribromethanol per kilogram by rectum, he became somewhat relaxed, but responded to the slightest stimulation of the cerebrum, and if spoken to, would sit up in bed and talk wildly. The slight effect of the drug passed off in less than two hours. Three days later, this patient was given 0.2 Gm. of sodium *iso*-amylthiobarbiturate.

intravenously, after which he slept soundly. The injection was continued to a total of 0.5 Gm of sodium *iso*-amylethylbarbiturate, with the result that the patient slept for seven hours, awoke, ate dinner and again slept or was quiet for eight hours.

Many other cases could be cited to show that tribromethanol is in effect primarily a somatic sedative, becoming a psychic sedative only in large doses. For this reason, we feel that scopolamine is a highly desirable adjuvant in combination with tribromethanol.

In view of the possibility of damage to the liver and kidneys from the use of tribromethanol, 2 cases of cholecystectomy in which a rather high degree of damage to the liver was present, and 5 of nephrectomy in which the other kidney was in none too good condition, were included in the aforementioned 100 cases. In each of these cases the patient made a satisfactory recovery. In each, oxygen was freely displayed through the pharyngeal airway throughout the operation.

*Amylene Hydrate Preparation*—A preparation at one time forwarded by the manufacturers, namely, a solution of tribromethanol in amylene hydrate, carried 1 Gm of tribromethanol per cubic centimeter. We used this preparation in place of the crystals for one month, with the following observations:

- 1 Amylene hydrate lends a distinctly unpleasant odor to the solution, and this odor is exhaled by the patient during anesthesia.

- 2 The mixing of this solution with distilled water we found to be nearly as difficult as was solution of the crystals of tribromethanol in distilled water. Small globules of amylene hydrate solution tended to remain separate and were less easily noted than was incomplete solution of crystals.

- 3 Measurement of a liquid by means of a pipet or graduated cylinder seemed less accurate in our hands than the handling of powders weighed out by the hospital pharmacist.

- 4 It seemed to us that a larger proportion of persons anesthetized with a 3 per cent solution of tribromethanol made by means of the amylene hydrate preparation showed irrationality and uncontrollable restlessness during recovery than of persons anesthetized by means of the crystal preparations and that the period of postanesthetic sleep for the former was longer. Unless there is a distinct advantage in convenience of manufacture and marketing in favor of the amylene hydrate preparation, we see no advantage in the introduction of a mixture of two active drugs when one will serve as well. A preoperative and postoperative proctoscopic study of the crystal and fluid preparations of tribromethanol is in progress.

*Intravenous Use of Tribromethanol*—Kirschner<sup>52</sup> recently suggested the intravenous use of this drug. A 3 per cent solution is made in physiologic solution of sodium chloride, and 1 cc for each kilogram of the patient's body weight is injected into a vein during an interval of forty-five seconds. Kirschner stated that anesthesia follows instantly and is complete, and that recovery occurs within fifteen minutes.

The startlingly rapid induction and recovery that we had previously noted in dogs when tribromethanol was given intravenously, together with the lack of symptoms following, led us to administer tribromethanol intravenously to seven patients in whom a temporary profound anesthesia was needed. Two were given 1 cc of 3 per cent solution of tribromethanol in physiologic solution of sodium chloride per kilogram of body weight. The injection was as rapid as possible. No premedication was used. In each patient, immediate anesthesia resulted, in one deep and in the other light. Both awakened ten minutes later. One ate his lunch on returning to the ward one-half hour after injection.

One patient was given a similar dose (1 cc per kilogram) without premedication, the injection being given slowly, and a light anesthesia was maintained for twenty minutes. A fourth case demanded deep anesthesia for fifteen minutes. The patient had just received one-sixth grain of morphine sulphate hypodermically. He was given 90 cc of 3 per cent solution instead of 63 cc, which was the calculated dose at 1 cc per kilogram. Profound anesthesia, with slow pulse and depressed respiration, lasted five minutes followed by deep anesthesia, with normal pulse and slow deep respirations gradually lightening to phonation and muscular movements twenty minutes after injection. He was awake twenty-three and one-half minutes after injection and asked for cigarettes. During the next four hours he complained of pain in the upper part of the abdomen whenever awake, but he slept a great deal during that time. He then ate dinner and vomited afterward. He also vomited his breakfast the next morning, and still complained of pain in the upper part of the abdomen. Later that day he was discharged from the hospital, feeling fit. No other case of abdominal pain or nausea occurred when anesthesia was produced by tribromethanol given intravenously. One patient, in whom two attempts had been made to obtain anesthesia with intravenous injection of tribromethanol, was found at the third attempt to have a thrombosis of each median basilic vein, extending several inches above the point of injection. No other instances of thrombosis have been noted.

Further study as to the safety of intravenous administration of tribromethanol is indicated. A method of producing complete, profound

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<sup>52</sup> Kirschner, M. Eine psycheschonende und steuerbare Form der Allgemeintäubung, *Chirurg* 1 673 1929

and extremely short anesthesia has possibilities of usefulness in carefully selected cases. The extremely rapid detoxication of tribromethanol when it is administered intravenously, is interesting.

### SUMMARY AND CONCLUSIONS

A review of the literature concerning tribromethanol is presented. Certain laboratory data are recorded verifying and extending the experi-

TABLE 4—*Statistics on One Hundred Cases in Which Anesthesia Was Obtained with Tribromethanol*

Average		
Age (range from 4 days to 74 years)		24 years
Weight		88 pounds (39.9 kg)
Calculated dose (3 per cent aqueous solution)		132 cc
Given dose		150 cc
Length of operative procedure		53 minutes
Length of supplemental anesthesia		25 minutes
Length of induction period		20 minutes
Duration of sleep		3½ hours
Patient morphinized		83 per cent
Patient nonmorphinized		17 per cent
Tribromethanol supplemented		71 per cent
With gas (nitrous oxid and oxygen)	50 per cent	
With procaine or cocaine hydrochloride	21 per cent	
Tribromethanol unsupplemented		29 per cent
Respiratory and Circulatory Changes		
Pulse—Rise or fall more than 20 per minute from normal		13 per cent
Systolic—Rise or fall more than 20 mm Hg from normal		11 per cent
Respiration—Under 20 per minute		2 per cent
Between 20 and 30 per minute		70 per cent
Over 30 per minute		28 per cent
Shock		2 per cent*
Recovery		
Nausea or vomiting (72 hours)		22 per cent†
Marked restlessness		12 per cent
Distention		5 per cent‡
Marked perspiration		4 per cent
Headache (nasal)		3 per cent
Deaths		2 per cent§

\* One, a patient operated on for tumor of the brain the other, a woman brought to the operating room with streptococcus septicemia secondary to neglected infection of the abdominal wall.

† Seventeen per cent of these were cases in which the patient swallowed blood in the course of an operation on the mouth or the face.

‡ All were cases in which laparotomies or nephrectomies were done, the distention occurring on the third day following operation.

§ A patient with tumor of the brain who died ten and a half hours following operation and one with a cleft palate, who died three hours following operation.

mental work of previous investigators. The points of major interest are

1. When kept at ordinary room temperatures, 3 per cent solutions of tribromethanol are stable toward hydrolysis for a period of approximately from twenty-four to forty-eight hours following their preparation.

2. Anesthesia obtained with tribromethanol in animals indicates that the drug has approximately the same margin of safety as other drugs commonly used in the production of general anesthesia. The anesthetic dose is approximately from two thirds to three fourths of the fatal dose.

3 Animals in which anesthesia has been obtained repeatedly show no noticeable variations in susceptibility to the narcotic action of the drug. Following repeated anesthesia, dogs show pathologic changes in the kidneys, liver and spleen. The type of lesion is not that characteristic of the intoxication caused by chloroform.

4 Tribromethanol acts as a prophylactic against the convulsive effect of toxic doses of procaine hydrochloride and cocaine in rabbits. Under tribromethanol anesthesia the fatal dose of these local anesthetics is increased from 50 to 200 per cent, respectively.

Record is made of our experiences with the clinical administration of this drug in 100 cases. The patients represented a wide range of surgical risks, in order to afford a fair test of the usefulness and safety of the drug. Analysis of these experiences leads us to the following conclusions:

1 As does the use of other anesthetic agents administered orally, intravenously, subcutaneously and rectally, the use of tribromethanol necessitates a predetermined dosage, which involves an element of chance as to the proper amount to be given to each individual.

2 If proper precautions are observed in the preparation of solutions, we feel that we can safely administer the drug in doses not exceeding 0.1 Gm. per kilogram of the individual's body weight, in most cases.

3 Since tribromethanol is a somatic rather than a psychic depressant, we feel that proper psychic depression with such drugs as scopolamine administered hypodermically or derivatives of barbituric acid administered orally should precede its use in cases in which anxiety is a factor. Moderate doses of opium derivatives can wisely be used as adjuvants. This combination of hypodermic, oral and rectal administration should preferably accomplish an effect short of complete surgical anesthesia.

4 Nitrous oxide with an excess of oxygen has been found satisfactory in the accomplishment of final anesthetic control.

5 An artificial pharyngeal airway for the maintenance of free breathing through the relaxed pharynx is essential in every case. Oxygen flowing through the airway is of distinct benefit to the patient.

6 The absence of gastro-intestinal irritation, together with the freedom with which oxygen can be administered, accompanying this agent, appears to make its use justifiable in cases of severe damage to the kidneys and liver, provided minimum dosage is employed.

7 No advantage appears to result from the use of tribromethanol "fluid" (67 per cent tribromethanol + 33 per cent amylene hydrate) in place of crystalline tribromethanol for the preparation of anesthetic solutions. In our hands, the crystalline form of the drug gave more

satisfactory results than the amylene hydrate solution. As noted before a comparative proctoscopic study of the possible rectal irritation from the crystal and fluid forms of the drug is in progress.

8 Alterations in blood chemistry under anesthesia from tribromethanol as herein described, are probably not clinically significant.

9 The only antidote for overdosage so far found useful is maintenance of a free airway and administration of oxygen, with the addition of small amounts of carbon dioxide when indicated. In extreme overdosage artificial respiration with oxygen should be utilized.

10 The possible usefulness of tribromethanol administered intravenously in extremely short operations deserves trial and investigation in view of the pleasant and quick induction and recovery without gastro-intestinal disturbance.

11 The need for experience and careful attention on the part of the anesthetist as to dosage and supervision is in no way less than with the agents now in common use.

12 Justification for the addition of tribromethanol to the present well recognized list of anesthetic drugs probably rests chiefly on the fact that it brings one a step nearer perfect induction of anesthesia. Induction by means of a simple, nonpainful rectal instillation without preparation with other drugs fills a need in the present armamentarium.



# BLUE-DOMED CYSTS AND CANCER OF THE BREAST \*

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The etiology of cysts of the breast furnishes a field for interesting speculation, and many theories have been advanced to explain their origin and development<sup>1</sup> Cheatle's<sup>2</sup> study of sections of the entire breast shows the relation of cysts to the epithelium of the ducts and acini

Two varieties of cysts may be separated according to the character of the cyst wall In the first, the wall is lined by one or more layers of epithelial cells, and either is smooth or shows papillary ingrowths In the second, the epithelial lining is absent or fragmentary and degenerative

In the first variety the cysts are small, multiple tumors which contain clear, cloudy, milky or bloody fluid The epithelial lining of these cysts is derived more often from the duct than from the acinus, and the cysts are due not to mechanical obstruction from the outside, but to epithelial proliferation in the duct In the second variety the cysts are large, clinically, they usually are single tumors, when exposed by an incision, they appear as blue, smooth, rounded masses, an appearance which gives them the name, blue-domed cyst

With obstruction, secretion from the epithelium fills the lumen of the duct and acinus with fluid of varying quality Accumulation of the fluid distends the obstructed area and produces a mass more or less spherical in outline If the distention is sufficient, pressure within the spherical cyst interferes with the nutrition of the epithelium, so that this portion of the wall becomes fragmentary or disappears During this time, chemical changes taking place in the accumulated fluid alter its character When the epithelium of the cysts is of direct origin, the breast about the cysts will contain many dilated ducts, but dilatation of the acini is not necessarily present

The papillomatous cyst contains bloody fluid or grumous material Cheatle declared that he had never seen a breast that contained only a single cyst With the papillomatous cysts this is an important fact, because these tumors undoubtedly have malignant potentialities

There is no evidence that the smooth-walled epithelial-lined cyst is prone to malignancy, and there is no evidence that the danger is proportional to the size of the cyst, but it has been found that any sized cyst may contain papilloma and primary carcinoma

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Submitted for publication, March 25, 1930

1 Goldzieher M A, and Kaldor, J Cystic Cirrhosis of the Breast, Arch Surg 20 473 (March) 1930 Rodman, J Stewart Chronic Cystic Mastitis Preliminary Report of the Nature of the Process Arch Surg 20 515 (March) 1930

2 Cheatle Brit J Surg 8 149 (Oct) 1920, ibid 9 235 (Oct) 1921

The blue-domed cyst from the wall of which the epithelial lining has disappeared cannot become the seat of cancer. Because this tumor is benign and so seldom associated with carcinoma, extremely conservative methods of treatment have been recommended. Many years ago Abbe<sup>3</sup> advised aspiration of the cysts, but the method was soon abandoned, because it gave no opportunity for examination of the wall of the cyst or the surrounding breast tissue. Recently, Bloodgood<sup>4</sup> advised that when a patient whose original tumor is a blue-domed cyst, comes back with a similar lump in the same or the opposite breast, it is his rule not to reoperate.

The clinical signs of blue-domed cyst are fairly distinct, and usually the diagnosis can be made with a reasonable degree of accuracy. The tumor is spherical, often fluctuates and is not fixed in the tissues. The surrounding breast is lumpy rather than shotty and it is rare to find dilated ducts beneath the nipple. Transillumination of the breast shows a clear area in the position of the tumor. Often the tumor is painful or tender and there is a history of variation in its size at different times. Sometimes there is a clear history of the spontaneous disappearance of a similar tumor followed by the development of the one under investigation.

In spite of these distinct characteristics, no clinical examination can show the condition of the cyst wall. In certain rare instances the wall contains an area of active epithelium, which is potentially malignant. Adams<sup>4</sup> reported a case in which cancer developed in such an area in a blue-domed cyst. Bloodgood admitted that cancer was present in 1 per cent of his 500 cases, but pointed out that in these cases the malignant tumor was diagnosed before operation. In a series of 100 cases of cancer of the breast, I have had 3 in which carcinoma and blue-domed cyst were present at the same time, in these cases the cancer was recognized by clinical signs but there must have been a period in the course of the disease when it was not so evident. Therefore it is better to excise all blue-domed cysts and to study the surrounding breast tissue as well as the wall of the cyst for areas of malignancy.

The large cyst practically never is a single tumor, and all the small cysts contain actively proliferating epithelium, with or without papillomatous ingrowths. Our experience with papillomatous cysts has not been as encouraging as Dr. Bloodgood's.<sup>5</sup> In a series of 100 cases of cancer of the breast, 5 showed cancer developing in a papillomatous cyst.

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3 Bloodgood, J. C. Blue-Domed Cyst in Chronic Cystic Mastitis. Its Relation to Cure of Cancer, to Benign Lesions of the Breast and to Educational Program, *J. A. M. A.* **93** 1056 (Oct. 5) 1929, The Blue-Domed Cyst of Chronic Cystic Mastitis in the Breasts of Women, *ibid.* **93** 1163 (Oct. 12) 1929.

4 Adams. *Canad. M. A. J.* **19** 190 (Aug.) 1928.

5 Bloodgood. *Am. J. M. Sc.* **179** 32 (Jan.) 1930.

In 8 benign papillomatous cysts all the specimens showed the presence of multiple growths. One specimen was the second breast removed from a patient who had been operated on for carcinoma in the other breast. The cancer in the first breast was an infiltrating scirrhous in the nipple zone.

One woman who had a bloody discharge from the nipple was examined at monthly intervals for more than a year, and no palpable tumor could be found. She returned six months later with a tumor in the nipple zone, which was clinically malignant. She was operated on by another surgeon, who reported that the tumor was a carcinoma in a papillomatous cyst. In dealing with cysts of the breast too great conservatism is dangerous. In my opinion, the blue-domed cyst as well as the papillomatous cyst should be excised in all instances, and the cyst wall carefully studied.

With recurrent blue-domed cysts, repeated excisions may become necessary, and in instances of recurrence, therefore, removal of the breast should be advised. These patients usually are at the menopause, the breasts are small, and the removal of one or both is a slight disfigurement. The 1 to 3 per cent possibility of concurrent malignancy is thus avoided.<sup>6</sup>

The following is a summary of the records in three instances of the simultaneous presence of cancer and blue-domed cyst of the breast.

#### REPORT OF CASES

CASE 1—A white woman, aged 48, was admitted to the hospital on Sept. 22, 1925. She was married but had never been pregnant. The duration of the tumor was six months. There were two smooth, rounded masses just below and to the outer side of the nipple, extending into the upper inner quadrant of the left breast. To the inner side of these masses there was a hard, sharp-edged tumor, about 1 inch (2.5 cm.) in diameter, over which the skin dimpled when the breast was lifted forward from the chest wall. The right breast was free from lumps. General clinical examination was negative for evidence of other lesions.

The complete operation for cancer was performed on September 24. The note made at the time of operation mentioned that fibrosed lymphatic glands were found in the axilla, but that the vein was not adherent. The wound was closed with a skin defect on the chest wall, which was covered with pinch grafts six days later. The patient made a good recovery and was discharged on the twentieth day following operation.

The tumor was a scirrhous carcinoma about 1½ inches (3.8 cm.) in diameter, with infiltrating projections for a considerable distance in all directions. On the inner side of the cancer between it and the skin about the nipple, there were two large blue cysts, each about 1½ inches in diameter. Both cysts were fixed to the carcinoma, but apparently the fixation came from infiltration of the cyst wall by

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<sup>6</sup> Fischer, W. Clinical and Pathologic Anatomic Diagnosis of Tumors and Cystic Transformation in the Mammary Gland, *Deutsche Ztschr. f. Chir.* 192 1, 1925.

the carcinoma rather than from extension of a primary tumor from the cyst wall

On Jan 25, 1926, a little more than three months later, she returned with a mass in the right axillary prolongation of the right breast. She had noticed the tumor while bathing the day before. The tumor was clinically malignant, hard, sharp-edged and fixing the skin. The complete operation was performed on the right side on January 27. The axilla appeared favorable, the wound was closed with a skin defect, which was grafted four days later. The patient again made a good postoperative recovery and was discharged on Feb 16, 1926.

The tumor from the right breast was a small, infiltrating scirrhous. Just beyond the tumor toward the axilla there was blue-domed cyst about 1 inch in diameter, and around the solid cancer there were a number of small blue cysts. At no place could a connection between the cancer and the walls of a cyst be found.

The patient remained well for about a year, and then began to show signs of metastasis of the spinal roots. She died with evidence of general carcinosis two years after the first operation.

CASE 2—A colored woman, aged 38, was admitted on Oct 19, 1928, complaining of lumps in the right axilla. There were three separate masses, the lowermost one being on the border of the pectoralis major at the base of the axilla and the others higher up in the space. The masses were smooth and a little tender, and the lowermost one was attached to the skin for a short distance. There were no lumps or tender areas in the breast and no wounds or scars of the hand or arm.

General clinical examination gave negative results, and laboratory tests threw no light on the probable nature of the masses.

At operation the upper smooth masses were found to be blue-domed cysts, and the lower one a papillomatous cyst, containing blood and showing an indurated and infiltrating wall. The complete operation for cancer was performed. The fat along the axillary vein was soft, and no fibrosed lymphatic glands were noted. The wound was closed without grafting. The patient made a good recovery, and when seen one and one half years later was well.

No tumors were found in the normally situated breast tissue. The blue cysts and the malignant papillomatous cyst were situated in an axillary mass of breast tissue, which appeared to be a separate development rather than an extension of the axillary prolongation of the breast. The wall of the blue-domed cyst was distinct from that of the papillomatous cyst, and there was no infiltration between them.

Supernumerary breasts and aberrant masses of breast tissue are well known congenital anomalies. The unusual breast tissue often does not attract attention until it hypertrophies during lactation or becomes involved in tumor formation.

The axilla is a frequent seat of accessory breasts. As a rule, the supplementary tissue can be identified without question. McFarland<sup>7</sup> pointed to the close resemblance between the large sweat glands of the axilla and mammary tissue as a possible source of error in determining the nature of an axillary tumor. In the present case the blue cysts as well as the papillomatous one seemed to be definite indications that the tumor originated in breast tissue.

<sup>7</sup> McFarland. *Am J Path* 5 23 (Jan) 1929.

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<sup>7</sup> McFarland. *Am J Path* 5:23 (Jan) 1929.

# SKELETAL METASTASES FROM CARCINOMA OF THE RECTUM

REPORT OF EIGHT CASES \*

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NEW YORK

Since the advent of the widespread use of the roentgen ray for diagnosis, there has been a great increase in the knowledge of those neoplasms that cause osseous metastases. Carcinomas of the prostate, breast, thyroid and pulmonary bronchus, as well as hypernephromas, have been known to be the most common producers of secondary growths in the skeletal system. Primary carcinomas of other organs do cause metastases in the bones, and these occur with sufficient frequency to make their clinical recognition an important factor in the amelioration of their symptoms.

Skeletal metastases occur in 10.5 per cent of rectal carcinomas according to Nisnjewitsch,<sup>1</sup> who found them in six of fifty-seven post-mortem examinations. The determination of the true percentage of such occurrences is impossible from either a clinical or a pathologic standpoint unless the material is examined carefully with that point in view. Miyauchi<sup>2</sup> examined the lumbar vertebrae in thirty-five consecutive post-mortem examinations of patients with cancer and found five with gross metastases, in another five, metastases were found only on microscopic examination.

Skeletal metastases were found in 8 cases of rectal carcinoma at Montefiore Hospital during the period from Jan. 1, 1922, to March 1, 1930. During this time 117 patients were admitted with the diagnosis of carcinoma of the rectum. Of these, 78 died in the hospital and there were 29 autopsies. A careful search of the literature revealed only 16 reported cases of bone metastases in carcinoma of the rectum.

The first case of rectal carcinoma with bone metastases was reported by Curling<sup>3</sup> in 1870. This occurred in a man 48 years of age, who had

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\* Submitted for publication, April 14, 1930.

\* From the Surgical Service, Montefiore Hospital. Dr. Harold Neuhoef, Chief of Division.

1 Nisnjewitsch, Leo. Die Metastasen des Karzinoms in das Knochensystem, Inaugural Dissertation, Basel, 1907.

2 Miyauchi, K. Zur Kenntnis der Karzinommetastasen im Knochensystem, Inaugural Dissertation, Basel, 1916.

3 Curling, T. B. Case of Cancerous Stricture of the Rectum Producing Obstruction, Successfully Relieved by Colostomy, *Lancet* 1 3, 1870.

had a colostomy performed for rectal obstruction seventeen months before death. The postmortem examination showed a cancer of the rectum invading the posterior wall of the pelvis and sacral plexus. "A large tumour had formed at the right elbow which seemed to be a deposit of soft cancer in the upper part of the radius distending the bone."

Hildebrand,<sup>4</sup> in discussing statistics of rectal carcinoma, reported the case of a man, aged 59, with a history of having had the condition for eighteen months, in whom metastasis developed in the upper end of the femur seven months following proctectomy. Hochenegg<sup>5</sup> reported a case in which a Kraske resection had been performed and in which the patient nine months later had a spontaneous fracture of the right scapula due to metastasis. In addition to this fracture, the presence of metastases to the lungs, liver, peritoneum, kidney and suprarenal glands was confirmed post mortem. Both of these cases were reported in 1888.

In 1891, Pitts<sup>6</sup> reported a case of spontaneous fracture of the right humerus eighteen months after colostomy for intestinal obstruction due to rectal carcinoma. Because of pain and nonunion, amputation was done at the shoulder joint, with uneventful recovery. Pathologic examination revealed "a columnar cell carcinoma so perfect in character that it would be impossible to distinguish it from a similar growth in the rectum."

Fuzinami,<sup>7</sup> in 1897, described a case of spontaneous fracture of the femur after the patient had complained of pain in the bone for two months. There had also been diarrhea and an enlarged liver. At post-mortem examination, a cylinder cell carcinoma of the rectum was found with metastases to the liver and femur. The growth in the femur was of the same type as that found in the rectum. The author remarked that, according to his experience, such a metastasis was among the greatest of rarities.

In 1906, Goetsch<sup>8</sup> reported a case of metastases to the ribs, vertebrae and femur from a rectal carcinoma. Oehler,<sup>9</sup> in discussing the results of

4 Hildebrand, O. Zur Statistik der Rectumcarcinoma, Deutsche Ztschr. f. Chir. **27** 329, 1887-1888.

5 Hochenegg, J. Die sacrale Methode der Exstirpation von Mastdarmkrebsen nach Prof. Kraske, Wien klin. Wchnschr. **1** 348, 1888.

6 Pitts, B. Columnar Carcinoma of the Humerus Following Tumour of the Upper Part of the Rectum, Tr. Path. Soc. London **42** 267, 1891.

7 Fuzinami. Casuistische Mitteilung primäre Rectumbrebe mit Spontanfractur linken Oberschenkelknochen, Arch. f. path. Anat. **147** 129, 1897.

8 Goetsch, W. Ueber den Einfluss von Karzinommetastasen auf das Knochengewebe, Beitr. z. path. Anat. u. z. allg. Path. **39** 218, 1906.

9 Oehler, J. Ueber Rectumcarcinome zugleich ein Beitrag zur Lehre von den metastatischen Darm Carcinomen, Beitr. z. klin. Chir. **87** 593, 1913.



operative intervention on rectal carcinoma, mentioned one case in which six years after operation, without any local recurrence, metastatic growths in the pelvic lymph nodes and a large secondary tumor of the occipital bone developed

Mielecki,<sup>10</sup> in reviewing 560 autopsies in cases of cancer found 3 metastases to bone in 56 intestinal carcinomas. One of the cases was a rectal neoplasm. Deelman,<sup>11</sup> in reporting 27 cases of bone metastases from various primary tumors, found 1 from a rectal carcinoma, the site of metastasis was in the vertebrae.

Mandl,<sup>12</sup> in reviewing 779 operations for rectal tumor in Hochenegg's clinic from 1906 to 1920, found 3 cases of bone metastases in 64 postmortem examinations, 1 to the sacrum and spine, 1 to the ribs and 1 to the sternum. He felt that there had been a great increase in the number of bone metastases in later years, and ascribed it to a lessened resistance of the human organism.

Joll<sup>13</sup> described three specimens in the British Museum of osseous metastases from rectal carcinomas. The one specimen is the early case described by Pitts, the second, metastasis to the sternum and spine in a patient 35 years of age, and the third, a metastasis to the ulna.

Jenkinson,<sup>14</sup> in reviewing skeletal growths secondary to malignant intestinal (all parts) conditions, cited among the rectal cases those of Goetsch and Deelman and added one of his own with metastasis to the spine. Jacobs,<sup>15</sup> who reviewed the cases at Montefiore Hospital from 1914 to 1924 in respect to roentgen therapy, mentioned that bone metastasis occurred in four. Siburg,<sup>16</sup> in 1929, reported a case of carcinoid of the rectum with metastases to the lymph nodes and to the thoracic and lumbar vertebrae.

#### REPORT OF CASES

CASE 1—S. L., a man, aged 44, was admitted to the hospital on Aug. 24, 1921, with a history of blood in stools, difficulty in moving bowels and painful defecation for four years. He had had a rectal operation four years before.

10 von Mielecki, W. Anatomisches und kritisches zu 560 Obduktionen bei denen sich bosartige Geschwulste fanden, *Ztschr. f. Krebsforsch.* **13** 505, 1913.

11 Deelman. Het metastatisch carcinoom in het beenstelsel, *Nederl. tijdschr. v. geneesk.* **65** 1048, 1921.

12 Mandl, F. Ueber den Mastdarmkrebs, *Deutsche Ztschr. f. Chir.* **168** 145, 1922.

13 Joll, C. A. Metastatic Tumours of Bone, *Brit. J. Surg.* **11** 38, 1913-1924.

14 Jenkinson, E. L. Primary Carcinoma of the Gastro-Intestinal Tract Accompanied by Bone Metastases, *Am. J. Roentgenol.* **11** 411, 1924.

15 Jacobs, A. W. Carcinoma of Rectum and Sigmoid. Analysis of 121 Cases, Results of Treatment by Radiation, *Surg. Gynec. Obst.* **43** 50, 1926.

16 Siburg, F. Ueber einen Fall von sogenannten Carcinoid des Rektums mit ausgedehnter Metastasenbildung, *Frankfurt Ztschr. f. Path.* **37** 254, 1929.

admission, which was followed by good health (except rectal incontinence) until February, 1921. Colostomy was performed in May, 1921. For two weeks before admission, he had pain in both legs. Examination showed a fairly well nourished man who had had a left inguinal colostomy. There was a scar from a former rectal operation with resection of part of the sacrum. There was a hard, nodular, polypoid mass protruding from the anus, with hard nodules in the skin. The anal orifice did not permit insertion of finger. There was an enlargement of the left inguinal glands.

Roentgen examination on Sept 7, 1921, revealed "several small, irregular areas of bone absorption within the right os ischi and a small, irregular area of bone absorption in the infratrochanteric region of the left femur. These areas are characteristic of metastatic growths." A painful area with swelling developed over the upper part of the sternum. On Dec 28, 1921, the roentgen rays revealed a circumscribed area of bone condensation the size of a half dollar, occupying the middle third of the sternum. The patient slowly became worse, and died on Jan 9, 1922.

Autopsy revealed a carcinoma of the rectum with an extension into the pelvic tissues and metastases to the regional and distal lymph glands, lungs, calvarium, dura, heart, capsule of the left kidney, ribs, sternum, lumbar vertebrae and sacrum. Bilateral hydro-ureter and hydronephrosis due to ureteral obstruction by tumor tissue was revealed.

CASE 2—C B, a man, aged 50, was admitted to the hospital on June 29, 1923, with a history of chronic colitis and rectal polyposis for fourteen years. Colostomy had been done in 1910 for the relief of colitis. The patient had had pain in the right foot, back and spine for three months before admission.

Examination revealed an enlarged liver and enlarged inguinal glands. Examination of the rectum revealed large nodular, infiltrating carcinomatous masses. A biopsy specimen was reported to show adenocarcinoma.

Roentgen-ray examination on July 5 showed small areas of bone destruction and marked osteoplastic changes especially involving the right half of the sacrum and contiguous portions of the ilium. The lumbar part of the spine and the lungs were negative for metastases.

The patient gradually lost weight and strength, and died on Aug 11, 1923.

CASE 3—S T, a woman, was admitted to the hospital on Feb 26, 1924. She had a combined Kraske operation in May, 1921, for an adenocarcinoma of the rectum with colloid degeneration. The patient was delivered of a normal child, in February, 1923. In August, 1923, active tuberculosis of left upper lobe developed. The patient was sent to Bedford Sanitarium on March 22, 1925. There were pain in the rectum, blood in the stools and diarrhea. In May, both gluteal regions were involved by carcinomatous tissue.

Roentgenograms of the pelvis taken on April 26, May 29 and September 11 were negative for metastases. Roentgenograms of the skull on Feb 17, 1926, showed no metastases. The patient died on May 23.

At autopsy, colloid carcinoma of the rectum and metastases to the ribs and vertebrae were revealed. All ribs showed extensive tumor infiltration, in places they were swollen to twice their normal thickness. Metastases to subcutaneous and muscular tissues of the back, lungs, liver, kidneys, peritoneum, suprarenals, skin, brain and heart were found. There was obstruction of the left ureter with hydro-ureter and hydronephrosis. Pulmonary tuberculosis was revealed.

CASE 4—W B, a man, aged 61, was admitted to the hospital on Aug 7, 1926. Three years before admission, the patient had blood in stools had lost

weight and was weak. In 1924, colostomy was done and later a vesicocolonic fistula was made to relieve vesical obstruction.

On examination, the patient presented an enlarged liver and enlarged, hard inguinal glands. Over the anterior part of the chest, there was an "encrasse" of the tissues. A stony hard induration around the external sphincter prevented insertion of even the little finger. On Sept. 1, 1926, the patient suffered a spontaneous fracture of the right humerus.

The roentgen rays showed a pathologic fracture at the middle third of the shaft with an extensive area of bone destruction about 6 cm. in length at the site of the fracture. A roentgenogram of the chest showed pulmonary metastases. The patient died eight days later.

Autopsy revealed carcinoma of the rectum with metastases to the regional lymph nodes, lungs, liver, kidney, suprarenals and skeleton, pathologic fracture of the right humerus, an irregular, flat elevation, 2 by 3 cm., on the lateral surface of the fourth right rib, adherent to a large mass on lateral surface of right middle lobe, tumor nodules on the inner surface of several ribs. These nodules were not adherent to the lung.

CASE 5—J. B., a man, aged 50, was admitted to the hospital on Jan. 22, 1927. One year previously, he had complained of abdominal cramps. In July, 1926, he had severe pain in the lower part of the back. Hemorrhoidectomy was performed. In September, he had a rectal hemorrhage, accompanied by weakness and loss of weight. Colostomy was done in October.

Physical examination revealed a ridge of hard, immovable tissue extending from the anus along the perineum. Three centimeters from the anal orifice, the rectal circumference was involved by firm tissue, and 6 cm. from the anal orifice, the entire rectal lumen was obstructed. The left eighth, ninth and tenth ribs were prominent and tender. Roentgenograms of the skull and chest were negative for metastases. The patient died on March 6, 1927.

Autopsy revealed adenocarcinoma of the rectum with metastases to the regional lymph nodes, liver, lungs, ribs and suprarenals. The right eighth and left sixth ribs were invaded by metastatic tumor nodules.

CASE 6—H. B., a man, aged 47, was admitted to the hospital on Jan. 15, 1928, with the history of having blood in the stools and rectal pain three years previously. Two years before admission, carcinoma of the rectum was diagnosed and colostomy done. In September, 1927, pain in the left leg developed. This pain was thought to be due to the enlarged inguinal glands, and they were given considerable roentgen therapy. A roentgenogram of the pelvis in October, 1927, was negative for metastases.

Physical examination on admission revealed a hard, moderately tender swelling over the middle of the left thigh about 8 cm. in diameter and attached to the bone. The left inguinal glands were enlarged and tender. Rectal examination revealed two large tumor tabs protruding from the anus, with numerous firm nodules in the rectum extending as high as could be reached.

A roentgenogram of the chest in January, 1928, was negative for metastases. A roentgenogram of the left femur taken in January, 1928, showed a thickening of the periosteum and a moderate amount of bone absorption in the middle third of the shaft. In April, 1928, roentgenograms showed an increase in the bone destruction of the left femur with invasion of the soft parts by a tumor mass extending to the inner and outer side of the shaft. Roentgenograms of the spine, pelvis, skull and humeri were negative for metastases. The patient died on June 15.

Autopsy revealed a colloid small cell carcinoma of the rectum with metastases to the retroperitoneal lymph nodes and inguinal glands, skin, liver, gallbladder and

left femur The mass around the left femur stripped freely from the bone, but the cortex of the femur was thickened, finely nodular and of increased density A segment of bone was not removed The tumor mass had a gelatinous appearance, and through this portion were scattered numerous spicules of bone

CASE 7—N S, a man, aged 63, was admitted to the hospital on June 10, 1928, with a history of pain in the rectum, mucous rectal discharge and diarrhea for six months A colostomy had been done eight weeks prior to admission, and biopsy at that time showed a malignant adenoma The patient had complained of a pain in the back for four weeks

Examination revealed a large, hard mass completely obstructing the rectum A roentgenogram taken on June 12 showed an irregular area of bone absorption in the upper end of the right femur, characteristic of early metastatic growth The patient died on September 9 of a rectal hemorrhage

Autopsy revealed a colloid carcinoma of the rectum with hemorrhage metastases to the regional lymph glands and liver The femur was not examined

CASE 8—E C, a woman, aged 68, was admitted the hospital on Jan 8 1930, with a history of having had a sacral Kraske operation performed two years previously for adenocarcinoma of the rectum with lymph nodes involved The patient remained in good health for one year following operation, and then pain in the rectum developed Two months before admission she noticed a lump on the back of her head

Examination showed a large circumscribed cystic tumor over the occipital region with a hard nodule in front of it On January 17, the roentgen rays disclosed areas of bone destruction in the right half of the occipital bone and the posterior portion of the right parietal bone These areas were characteristic of metastatic deposits The pelvis, femora and humeri were negative for metastases There were some thickening and narrowing of the artificial anus, but no definite local recurrence could be felt The patient was discharged on February 12 to be followed in the outpatient clinic

#### COMMENT

In five of these eight cases, the presence of the skeletal metastases was proved by autopsy In another autopsy was performed, but the site of the metastasis could not be investigated In the three cases not proved by autopsy, the roentgen-ray observations were sufficiently typical to make a positive diagnosis In six cases the diagnosis was made clinically, and in the remaining two the secondary growths were not discovered or suspected until after death In practically all of these eight cases, as well as in most of those reported in the literature, the disease was of long standing, and as carcinoma of the rectum is known to spread slowly, even locally it is not surprising to find the skeletal metastases occurring late in the course of the disease

The site of metastases is of interest, because in the entire twenty-four cases the various bones are involved with practically the same frequency as originally described by von Recklinghausen<sup>17</sup> in his monograph on the formation of bone metastases The skeleton was the site of

17 von Recklinghausen F D Festschr der Assistenten zu Virchow zu 71st Geburtstag Berlin, 1891

metastases thirty-five times in these twenty-four cases The frequency and percentages were as follows

Vertebrae	8	22.8%
Femur	6	16.8%
Ribs	6	16.8%
Skull	3	8.4%
Sternum	3	8.4%
Humerus	2	5.7%
Pelvis	2	5.7%
Sacrum	2	5.7%
Radius	1	2.8%
Scapula	1	2.8%
Ulna	1	2.8%
	<hr/> 35	

Von Recklinghausen claimed that metastases to the bone are not due to the embolic blocking of a vascular channel in the bone by a large mass of malignant cells, but are caused by the periaxial stagnation of the neoplastic cells as they pass from the blood vessels outside of the bony structure into the vascular bed situated within the bone. The blood vessels around the bone are of changeable size, depending on stimuli such as temperature and activity, while the vessels within the bone are of fixed caliber. In this manner the blood is often carried from a narrowed peripheral vessel into a wider vessel within the bone-marrow. This change in size of the vascular bed would tend to stagnate the neoplastic cells and to favor their multiplication. After they had multiplied sufficiently, they would block the vascular channel and then extend outward to the periosteum through the foramina without necessarily eroding the cortex.

Owing to this manner of formation, bone metastases should occur most frequently in those bones subject to the greatest strain and stress as well as to changes in temperature. Von Recklinghausen claimed that according to this theory, the frequency of bone metastases in various parts of the skeleton would be as follows: vertebrae, femur and pelvis, ribs and sternum, humerus, skull, tibia, radius and ulna. Practically all statistics have in the main confirmed his original contention. Nisn-jewitsch,<sup>1</sup> in 169 metastases to the bone, found the following frequency: vertebrae, 28.9 per cent, sternum, 17.7 per cent, femur, 15.9 per cent, ribs, 14.7 per cent, humerus, 7.6 per cent, skull, 7.1 per cent, pelvis, 5.3 per cent, tibia, 1.1 per cent, clavicle, 1.1 per cent.

The importance of the clinical diagnosis of bone metastases is shown in cases 4 and 6. In case 4 a pathologic fracture might have been prevented if the presence of considerable destruction of the bone had been recognized. In case 6 for a number of months, the pain in the leg

was considered to be due to the enlarged inguinal glands, which were given roentgen therapy. As irradiation offers some relief from pain in these skeletal metastases, their occurrence should be kept in mind, and all pains in the bone investigated by means of the roentgen ray.

#### SUMMARY

1 A series of eight cases of rectal carcinoma complicated by skeletal metastases is added to the sixteen reported in the literature.

2 In the main, the site of the metastases conforms to the original table of frequency as stated by von Recklinghausen.

3 Metastases to the bone in carcinoma of the rectum occurs late in the course of the disease, but with sufficient frequency to make it of clinical significance and to make its early diagnosis of great importance in relief from pain and the prevention of fractures.

# THE VALUE OF DRUGS IN THE RELIEF OF ILEUS

AN EXPERIMENTAL STUDY \*

ALTON OCHSNER, M D

I M GAGE, M D

AND

R A CUTTING, M D

NEW ORLEANS

The classification of cases of ileus into mechanical and paralytic varieties or, according to a different terminology, dynamic and adynamic varieties, is a distinction of fundamental importance. The mechanical or dynamic variety, by definition, is characterized by some condition which physically prevents the normal progress of intestinal contents toward the anus. The relief of such a physical obstruction is essentially a surgical matter involving relief of intestinal kinking, division of bands of adhesions, removal of new growths, circumvention of constrictions by accessory openings between adjacent intestinal loops or other surgical procedures, according to the indications presented by the individual case. If the patient with such an obstruction comes to operation early, this purely surgical therapy is all that is required. In the paralytic or adynamic ileus, however, a different state of affairs exists. There may or may not be some physical hindrance to the passage of intestinal contents along the intestinal canal, depending on whether the ileus was paralytic from the beginning or developed on the basis of a preceding dynamic ileus. If the mechanical factor is still present, this, of course, must be overcome as a prerequisite to success in the treatment for the paralytic condition, but the relief of a mechanical ileus associated with a paralytic ileus is, of course, of no value in itself. The fundamental abnormality, at least in the early stages before profound toxemic and physicochemical changes have occurred, is one involving the contractility of the muscular tunics of the involved segment of intestine. Although restoration of normal motility to a segment of paralyzed intestine may or may not save the life of the patient, he certainly will not recover unless this state of affairs can be established. There is considerable evidence to support the view that patients suffering from intestinal obstruction may live for a considerable number of hours in spite of the fact that inevitably fatal organic or physiologic changes

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\* Submitted for publication, Feb 27, 1930

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have already developed. In this connection it is exceedingly significant that not infrequently patients with advanced paralytic ileus succumb promptly as soon as the ileus is relieved. Indeed, clinicians of experience do not view the resumption of peristalsis in an intestine that has been paralyzed for a considerable period of time with entire equanimity, since the patient may either become worse and die or may rapidly become improved and survive, depending probably on the amount of toxin previously absorbed, and the clinician has no available means of determining which direction the subsequent course of events may pursue. In any case, there is every reason for believing that any measure designed to restore movement to a paralyzed intestine will ordinarily be of value more or less directly in proportion to the promptness with which it is invoked. Perhaps it is hardly necessary to emphasize in this way the fundamental gravity of paralytic ileus, but in this paper we deal primarily with the value of drugs in the treatment for this type of ileus.

It is a matter of common knowledge that drugs, as a rule, are of relatively little value in combating the well established and graver forms of disease processes in general. It would seem in order, therefore, to emphasize the fundamental importance of the early recognition and early treatment for any abnormal process in which reliance is to be placed on drug therapy. In the following discussion of the usefulness of drugs in the treatment for paralytic ileus, all clinical and experimental evidence is considered solely in its relation to the case that has been recognized early. A large part of the experimental evidence about to be cited has been derived from observations on the behavior of normal or, at least, relatively normal musculature, and it would be gratuitous to assume that the reactions observed when dealing with normal or relatively normal muscle, are directly applicable to muscle that has been subjected to the changes incident to prolonged paralytic ileus. It should hardly be necessary to remark that the relief of ileus is not synonymous with the treatment for ileus, since the treatment for ileus involves not only restitution of normal movement to the intestinal tract, but also the combating of any associated abnormal process that may occur in connection with the paralysis. In this treatise we are concerned solely with a consideration of the use of drugs frequently considered beneficial in the stimulation of intestinal motility, drugs which presumably may be of value in restoring normal motility to a paralyzed intestine.

#### METHODS AVAILABLE FOR THE DETERMINATION OF THE ACTION OF DRUGS ON INTESTINAL MOTILITY

A number of different methods have been employed in testing the action of various drugs on intestinal motility.

The first and most fundamental of these involves the direct action of the drug on isolated portions of the intestinal musculature arranged



after the manner of the "Magnus" or "Trendelenburg" preparation. Usually the isolated strip of muscle has been immersed in an artificial blood serum like Locke's, Ringer's or Tyrode's solution to which a small amount of the test drug has been added. The effect on motility is recorded on a kymographic drum by means of a system of levers.

A second method, which is really a modification of the first, takes into consideration not only the muscular tissue as such, but also its intrinsic nerve supply, i. e., the plexuses of Auerbach and Meissner. The method is essentially the same as the first, except that instead of muscle alone, strips of muscular tissue which retain their intrinsic nerve supply are used. The two foregoing methods are obviously open to criticism in that the conditions involved are artificial. However, they have the advantage that they tend to reduce the number of experimental variables to a minimum.

A third method, and a much more physiologic one, makes use of an intact animal with a so-called Thiry or Thiry-Vella fistula. In this type of fistula a loop of intestine is isolated by transverse incisions made at some distance from one another, and the severed ends are stitched to the abdominal wall, making a permanent communication between the lumen of the segment and the body surface, continuity of the gastrointestinal tract is then restored. The loop of intestine thus isolated is made the subject of experimentation. The method has the advantage of preserving intact the nerve and blood supply to the loop of intestine under experimentation, but is unphysiologic in that the loop does not maintain its physical continuity with the intestinal tract. In determining the effect of drugs on intestinal motility, a balloon has ordinarily been placed within the lumen of the isolated segment, and intestinal motility has been recorded in the form of a tracing on the kymographic drum.

A fourth method consists in the observation of intestinal movement by means of the fluoroscopic screen. This method is more physiologic than the preceding one, but it is subject to two disadvantages. 1. An opaque substance must be present within the lumen of the intestine in order that a recognizable shadow may be produced. 2. The outline cast by the opaque material on the fluoroscopic screen is, at best, somewhat indistinct, and, therefore, subject to misinterpretation. Incidentally the personal equation introduced by the observer himself must be considered, as the method does not ordinarily permit the taking of reliable objective records.

A fifth method, if indeed it may be called a method at all, is that of the observation of clinical cases. The presence of borborygmi on auscultation of the abdomen and the appearance of flatus and feces at the anus are taken as presumptive evidences of intestinal motility. Although this method is the most physiologic of all, it is also the most unscientific. So many variables are present and the personal equation

is of so great importance that observations made when using such a method may be untrustworthy

A variation of the last method, which may conveniently be designated as a separate or sixth one, is the unaided ocular observation of the open abdomen either of experimental animals or of patients. The method is open to the same criticism as the last method with respect to the personal equation in addition to the criticism that the subject being subjected to study is under abnormal conditions.

A seventh method, the one that we have used in our experimental investigations, consists of laparotomy under a general anesthetic and the recording of intestinal movement by means of a balloon introduced into the intestinal tract at the time of or, at least, just preceding the investigation itself. This method is open to criticism (1) because the observations must of necessity be made under some form of anesthesia or analgesia, (2) because of unavoidable injury to the intestinal tract incident to the insertion of a recording device into the lumen of the intestine, and (3) because of the abnormality incident to the opening of the abdomen and consequent changes in pressure relationship and other physical influences. The last criticism may be overcome to a certain extent by opening the abdominal cavity within a bath of warm physiologic solution of sodium chloride, and the second criticism may be minimized, though not obviated, by gentleness and care in the use of the apparatus.

#### TECHNIC ADOPTED BY THE AUTHORS

Many different animals have been used by other investigators as subjects for experimental observation: rabbits, dogs, cats, guinea-pigs, rats and frogs. Our own observations have been made exclusively on dogs. Dogs are particularly suitable for use in experiments on intestinal obstruction, because in their intestinal reactions they simulate more nearly than most other animals, the reactions observed in the human subject. Many of the other common laboratory animals present fundamental organic differences in structure from those found in man and in any case many of them are too small to be conveniently used according to the technic adopted by us. The cat has been used somewhat extensively in experimental investigations of intestinal motility especially by Cannon and his co-workers<sup>1</sup> but this animal is unduly resistant to the production of intestinal obstruction and it is doubtful whether experimental results obtained by using such material would be directly applicable to cases in human beings. The rabbit, another animal frequently used in experiments on ileus and also for purposes of determining the action of drugs on intestinal motility, is a particularly

<sup>1</sup> Cannon W. B., and Murphy F. T. Physiologic Observations on Experimentally Produced Ileus. *J. A. M. A.* 49:840 (Sept 7) 1907.

poor experimental animal for use in experiments involving the observation or recording of movements of the gut. This animal, in addition to presenting anatomic peculiarities characteristic of the herbivorous animals, also presents a hyperactive intestine, and the ileus which is characteristically seen in many other animals including man, as the result of simple opening of the abdomen, is not seen in rabbits, the intestinal movement continuing in apparently uninterrupted fashion for minutes or even hours after laparotomy has been performed and frequently continuing for long periods even after the death of the animal had ensued. Experimental observations made on as excitable an organ as the intestinal tube of the rabbits would seem to be of relatively little value in their application to the human intestine.

Six-three animals were used in the experiments to be reported and the following drugs were employed: pituitary extract, physostigmine, peristaltin, pitocin, choline, acetyl choline and hypertonic sodium chloride solution. The method of procedure was as follows: The dogs were usually anesthetized with sodium barbital introduced by stomach tube, from 0.25 to 0.3 Gm. of the drug per kilogram of body weight being introduced in warm watery solution. When the animals had become anesthetic, as they did after a period of from one to three hours, the abdominal wall was incised to the peritoneum, care being taken to insure hemostasis, but the peritoneum itself was not disturbed. A midline incision was made in the neck and the trachea, the common carotid artery and the external jugular vein were exposed and isolated. The dog was then completely immersed, except for the head and neck, in a bath of saline solution heated to from 38.6 to 40 C. The temperature of the bath was maintained at this level throughout the experiment. A cannula was next introduced into the trachea, and connections were made between it and a recording tambour. The carotid artery was next cannulated, and by a system of rubber tubes filled with 2 per cent sodium citrate solution connections were made to a mercury manometer provided with a rider, lever and writing point. The external jugular vein was left exposed for the injection of the various drugs by hypodermic syringe and needle. The peritoneum of the animals was then incised and a loop of ileum near the ileocecal junction was carefully withdrawn. This intestinal loop was manipulated under water. A purse-string suture was placed in the wall of the bowel at its antimesenteric border, and a rubber tube terminating in a thin-walled rubber balloon was introduced for a short distance into the lumen of the intestine through an incision placed within the purse-string suture. The purse string was then tied tightly about the rubber tube. This rubber tube was connected to a tambour and writing point, a rubber bulb was provided by which air could be introduced into the intestinal balloon to produce any desired degree of initial pressure. In certain of the experiments normal animals were used, but in other experiments, animals in which experimental obstruction had been performed previously, the production of this artificial mechanical ileus was always made to precede the experimental observations by a period of forty-eight hours. For the production of obstruction, the abdomen of the animal was opened under ether anesthesia by means of a small low right rectus incision. The terminal ileum was located and was encircled by a piece of umbilical tape, the tape being tied sufficiently tightly to effect complete closure of the intestinal lumen but not sufficiently tightly to produce strangulation of the intestine at this point. In a number of animals in which the tape was tied too tightly, the animal succumbed.

to perforation and generalized peritonitis. The obstructed loop of intestine was replaced within the abdomen, the abdominal wound was sutured in layers, and the animal was allowed to recover. This procedure was, of course, performed under strictly aseptic conditions.

Using the technic previously described, tracings of the respiratory rate, the blood pressure and the intestinal movement were all obtained on a relatively narrow strip of kymographic paper. A long paper kymograph was used, and the drum was adjusted to revolve at a relatively low rate of speed so that observations could be continued over considerable periods of time, viz., from two to three hours. In certain of the experiments three balloons were inserted into the gut instead of one, the first balloon being inserted into the duodenum, the second into the ileum and the third into the colon. In the case of the animals that had undergone previously obstruction with tape, an additional opening was usually made into the terminal ileum, and a catheter was introduced in order to permit decompression of the dilated and fluid-filled intestine at that point and also to permit of observations on the efficiency of the various agents in actually extruding fecal material from the intestinal lumen.

Certain control experiments not specifically mentioned were made under ether anesthesia and others under local infiltration analgesia.

#### REVIEW OF THE LITERATURE

*The Action of Pituitary Extract*—Oliver and Schafer<sup>2</sup> are given credit for having introduced extracts of the pituitary gland into the practice of medicine by their demonstration of the action of extracts of this gland on smooth muscle. Largely because of the admitted stimulatory influence of pituitary extract on the smooth muscle of the uterus, it has been assumed that it has a similar effect on the smooth muscle of the gastro-intestinal tract, though this assumption has never been universally accepted. Bayer and Peter<sup>3</sup> found that extracts of the posterior lobe of the pituitary gland usually caused a stimulation of excised rabbit's gut after a preliminary period of inhibition. Houssay,<sup>4</sup> in 1922, was able to corroborate this observation on excised rabbit's gut as far as the stimulatory action of extract of the posterior lobe was concerned. In certain cases, however, he obtained inhibitions of intestinal movement, which he interpreted as being due to the action of chloretone contained in commercial preparations of the drug. He expressed the belief that chloretone-free preparations always act as stimulants. King and Church,<sup>5</sup> in 1923, using isolated preparations from the muscularis mucosae, found that when pituitary extract was applied to "cylinder" preparations, it caused definite shortening of the tissue, an effect which they had never been able to obtain by injecting pituitary

2 Oliver, G., and Schafer, E. A. *J. Physiol.* **18** 277, 1895.

3 Bayer, G., and Peter, L. *Arch. f. exper. Path. u. Pharmacol.* **64** 204, 1911.

4 Houssay, B. A. *Accion fisiologica de los extractos hipofisarios*, Buenos Aires, 1922.

5 King, C. E., and Church, J. G. *Am. J. Physiol.* **66** 428, 1923.

extract into living animals Cross,<sup>6</sup> using isolated pieces of the appendix taken from human patients at operation and suspended in Locke's solution at a temperature of 37 C., found that the addition of 0.5 cc of pituitary extract to the solution produced a slight increase in tone in the musculature Kaufmann,<sup>7</sup> in 1927, using a histamine-free preparation and one that did not contain chloretone found that concentrations of pituitary extract varying from 1:10,000 to 1:100,000 had no effect either on the duodenum or on the jejunum, however, such concentrations caused a definite stimulation of the ileum in both cats and rabbits The effect consisted of a definite increase in tone as well as an increase in the pendular movement and an increase in the frequency of this movement

In the case of the colon, concentrations of from 1:250,000 to 1:1,000,000 frequently produced a typical effect characterized by a preliminary phase of inhibition of tone and cessation of pendular movement, soon followed by a definite increase in tone and an increase in pendular movement Uno<sup>8</sup> found that a chloretone-free preparation of the posterior lobe of the pituitary gland had an inhibitory action on pendular movement and tone in the excised gut of the rat McIntosh and Owings<sup>9</sup> in 1928, working with animals subjected to experimentally produced intestinal obstruction and measuring the intra-intestinal tension by means of a special apparatus introduced into the gut, found that freshly prepared pituitary extract invariably showed a relaxing rather than a contracting effect on the intestinal musculature Brunner and Weigand<sup>10</sup> observed under the fluoroscope the large bowel of cats to which a barium sulphate enema had been given Pituitary extract was thought to be of little value in the stimulation of colonic movement Garry,<sup>11</sup> in 1927, found that only exceptionally was stimulation of the small bowel of the guinea-pig produced by injection of the extract of the posterior lobe or of the pars intermedia of the pituitary, and when stimulation was produced, it was but temporary

Concentrations of the drug of 1:1,000 or more characteristically produced inhibition of peristalsis, which was of long duration Ross,<sup>12</sup> in 1926, using a rubber balloon introduced into the intestinal lumen of a normal experimental animal, found that pituitary extract frequently

6 Cross, D. G. T. *Kerr Brit M J* **1** 9, 1924

7 Kaufmann, Margot. *Arch f exper Path u Pharmacol* **120** 322, 1927

8 Uno, T. *Am J Physiol* **61** 203, 1922

9 McIntosh, C. A., and Owings, J. C. The Effect of Solutions of Pituitary and Various Drugs on the Movements of the Small Intestine During Simple Mechanical Obstruction, *Arch Surg* **17** 996 (Dec.) 1928

10 Brunner, T. and Weigand, W. *Klin Wchnschr* **8** 1115, 1929

11 Garry, R. C. *Arch f exper Path u Pharmacol* **120** 348, 1927

12 Ross, J. W. *Canad M A J* **16** 241, 1926

failed to produce any motor response in the gut Voegtlin and Dyer<sup>13</sup> using rats as experimental animals, found that in chloretone and histamine-free preparations of extract of the posterior lobe both tone and pendular movement were inhibited Dixon<sup>14</sup> in 1923 found that although extracts of the posterior lobe of the pituitary caused stimulation of the small intestine an inhibitory action was produced in the colon MacDonald,<sup>15</sup> in 1925, stated the belief that although the action of extracts of the posterior lobe of the pituitary gland is essentially stimulatory to the intestinal musculature, this action is due especially to contamination with histamine, and that if this is removed, the stimulating action of the drug is largely destroyed Ross<sup>12</sup> found pituitary extract stimulating to rabbit's gut, and expressed the belief that when this effect is not seen, contamination with chloretone is responsible Degener<sup>16</sup> observed a characteristic inhibitory action of extract of the posterior lobe of the pituitary gland on the pendular movement of the small intestine in the rat Guggenheim<sup>17</sup> in 1914 found that pituitary extract produced stimulation of excised rabbit's gut, but that however if alkalis were added to the extract, the stimulating effect was not destroyed the stimulating effect on the uterine musculature however was destroyed by this procedure

Clinical reports on the efficacy of pituitary extract in the treatment for intestinal obstruction are rather abundant Blair Bell<sup>18</sup> was among the first to make use of and advocate the use of pituitary extract clinically for its effect on the intestinal musculature Bidwell<sup>19</sup> reported favorably on the routine postoperative use of pituitary extract for its effect on peristaltic activity For adults he advocated the use of 1 cc six hours after operation the dose to be repeated every four hours until eighteen doses had been given He credited this therapy with favorable results—the early passage of flatus marked absence of abdominal discomfort and satisfactory action of the bowel after the administration of an enema This report of course comes from the period in surgery when the early resumption of intestinal activity was considered a clinical desideratum and the surgeon became worried unless there was a copious bowel movement within the first twenty-four

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13 Voegtlin, C, and Dyer, H A *J Pharmacol & Exper Therap* **24** 101, 1925

14 Dixon, W E *J Physiol* **57** 179, 1923

15 MacDonald, A D *Quart J Exper Physiol* **15** 191 1925

16 Degener, L M *Am J Physiol* **60** 107, 1922

17 Guggenheim, M *Biochem Ztschr* **65** 189, 1914

18 Bell, Blair *Brit M J* **2** 1609, 1909

19 Bidwell L A *Investigation into Effect of Pituitary Extract on Bowels after Abdominal Operations*, *Clin J* **38** 351 (Sept 6) 1911 abstr *J A M A* **57** 1242 (Oct 7) 1911

hours postoperatively Duffey,<sup>20</sup> reporting from the same general period as the preceding author, stated that pituitary extract was used with favorable results in ten cases of postoperative stasis. It was the customary routine of this author to cause the patient's bowel to move within thirty-six hours after operation by the use of mild mercurous chloride and within forty-eight hours by the use of an enema. His advocacy of the method is dependent on his observation that the bowels would frequently move with the aid of pituitary extract, when they would not by routine methods.

Mayei,<sup>21</sup> in 1924, reporting on the use of pituitary extract in the treatment for postoperative ileus reported fifty-two cases, in thirty-six of which the injection of the drug was followed by defecation and the passage of flatus. Vogt,<sup>22</sup> reporting on the results of pituitary extract and intravenous salt solutions combined in the treatment for intestinal obstruction, stated that when this therapy is used favorable results are seen in that the pulse rate becomes slower and stronger, the blood pressure becomes increased, and usually within the course of from five to seven minutes the patient feels uncomfortable in the region of the abdomen and soon thereafter evacuates both gas and feces. He stated that pituitary extract affects the entire intestinal tract, and this he believed to be a factor of value in the treatment which he recommended. He considered that the saline solution is of value merely in diluting and causing the excretion of the toxin. He reported the recovery of fifteen patients in a series of eighty-one cases, a percentage of 22.2. He expressed the belief that if the intestinal tract does not respond to the use of hypophysin, the intestine is in a state of complete paralysis. Krinsky<sup>23</sup> in 1927, reported a severe case of ileus secondary to peritonitis, in which the pituitary-saline infusion of Vogt was believed to have saved the patient's life.

*The Action of Physostigmine*—Physostigmine is the active principle of the calabar bean. Physostigmine has been used clinically for its action on the intestinal tract for nearly fifty years. Frohner<sup>24</sup> is authority for the statement that physostigmine was originally used in veterinary surgery in the treatment for ileus in animals, for instance in colic, by Dieckerhoff in 1882. Westermann<sup>25</sup> reported the occurrence of tetanic contraction of the intestinal wall in cats, rabbits and dogs in

20 Duffey, R. New York M. J. **101** 72, 1915.

21 Mayer, A. Munchen med. Wchnschr. **71** 931, 1924.

22 Vogt, E. Munchen med. Wchnschr. **73** 1509, 1926.

23 Krinsky, A., and Stein, E. Zentralbl. f. Chir. **54** 591, 1927.

24 Frohner, E. Toxikologie fur Thierarzte, ed. 2, Stuttgart, Ferdinand Enke, 1900.

25 Westermann, W. Untersuchungen uber die Wirkungen der Calabarbohne, Dorpat, 1867.

from eight to ten minutes after the administration of 2.5 per cent glycerin solution of the alcoholic extract of the calabar bean and offered the hypothesis that this effect was due to stimulation of the sympathetic ganglions in the intestinal wall. Alvarez,<sup>26</sup> working with excised segments of rabbit's gut, observed that physostigmine, as well as certain other drugs, increased the tone of the musculature of the intestinal wall from the duodenum to the colon, whereas pituitary extract, which has been considered previously, characteristically presented a depressant effect on the rate of contraction. Cross,<sup>6</sup> using segments cut from the appendix removed at operation from human patients, found that physostigmine, when exhibited after pituitary extract, produced a very definite increase in the muscular tone, the pituitary extract itself producing only a slight increase. When the same two drugs were employed in the reverse order, there was relatively little effect. The use of pituitary extract following physostigmine produced only a relatively slight increase in tone. Baur,<sup>27</sup> using a Trendelenburg preparation and physostigmine salicylate, found that this drug produced little change in the tone of the intestinal musculature, but produced marked increase in the amplitude of peristalsis, especially in the longitudinal muscle fibers. On the basis of differences in action between the longitudinal and circular muscle responses, he expressed the belief that the action of the drug consists in increasing or changing the irritability of Auerbach's plexus. Ludlum and McDonald<sup>28</sup> in 1926, found in one clinical case that the administration of  $\frac{1}{64}$  grain (0.00101 Gm.) of physostigmine sulphate twice a day for six days produced a markedly contracted state of the colon, as shown on the fluoroscopic screen. LeHeux<sup>29</sup> in 1921, working by the roentgenographic method, found that physostigmine produced cramplike contractions of the gastro-intestinal tract.

Brunner and Weigand,<sup>10</sup> working by the fluoroscopic method and using cats, found that the exhibition of physostigmine produced a lively movement in the intestinal tract of these animals, which within from twenty to forty minutes resulted in active defecation. Oppenheim<sup>30</sup> working with rabbits and dogs, inflated the bowel through the rectum, opened the abdomen, made a small opening in the colon and then injected 0.003 Gm. of physostigmine salicylate. Immediately following the injection feces and gas were expelled from the colostomy opening. Twenty minutes after the injection the maximum action of physostigmine had been attained and the action of the drug was found to last from one half to three quarters of an hour. Baur<sup>27</sup> working with the

26 Alvarez Walter C. *Am J Physiol* **46** 554 1918

27 Baur, M. *Arch f exper Path u Pharmacol* **131** 233 1928

28 Ludlum S. D. and McDonald E. *M J & Rec* **123** 228 1926

29 LeHeux J. W. *Arch t d ges Physiol* **190** 301 1921

30 Oppenheim A. *Deutsche med Wchnschr* **28** 226 1902



alcoholic extract of the calabar bean in cats, found that the drug produced a marked spasmodic contraction of the entire gastro-intestinal tract from the stomach to the rectum, with the production of watery evacuations mixed with blood and mucus. Ross,<sup>12</sup> using experimental animals and a graphic method involving the introduction of a rubber balloon into the intestine, found that physostigmine was of greater value than pituitary extract in the stimulation of intestinal movement but he regarded even physostigmine as a relatively valueless drug. Traversa,<sup>31</sup> in 1899, working on the pharmacologic action of physostigmine, stated that the action of this drug on the intestinal tract is not modified by the exclusion of the medulla, the vagus and sympathetic nerves or the celiac ganglion. The contractions produced by the drug could be prevented or stopped, however, by the administration of atropine. Cannon and Murphy,<sup>1</sup> in 1907, injected physostigmine into animals in which ileus had been produced by crushing the testicle of the animal while under general anesthesia. Although in their experience the inhibition of the drug resulted in no hyperperistalsis in a normal animal, it produced a definite, though temporary, increase in peristalsis in animals so treated. Heller,<sup>32</sup> in 1883, reported the use of the calabar bean in combating constipation and flatulence due to atony of the intestines. Clinical cases showed favorable effects. Subbotin<sup>33</sup> used the extract of calabar bean and also the extract of *Physostigma* with good results in cases of atony of the bowel. Schaefer,<sup>34</sup> in 1880, reported good results from the use of the calabar bean in five cases of chronic constipation and flatulence. In the earlier years of the present century, a number of authors used physostigmine salicylate both as a prophylactic and as a curative measure in the treatment for postoperative ileus. As previously stated early postoperative evacuation of the bowel was considered desirable or almost necessary at that time. Noorden,<sup>35</sup> in 1901, reported favorably on the use of physostigmine, repeated at intervals in diminishing doses and beginning with 0.5 mg. Packard,<sup>36</sup> in 1902, reported a case of copious intestinal evacuation as the result of the injection of  $\frac{1}{150}$  gram (0.001 Gm.) of physostigmine salicylate, which was repeated in two hours, this was in a case of intestinal obstruction. In 1904, Packard<sup>36</sup> recommended the injection of 0.001 Gm. of physostigmine sulphate immediately postoperatively. He expressed the opinion that the action of the drug persists for three or four hours. The beneficial results obtained from the use of the drug were absence of distention and

31 Traversa, G. Polichnico 5 1, 1898

32 Heller, A. Deutsche med. Wchnschr., 1883, p. 123

33 Subbotin. Deutsches Arch. f. klin. Med., 1869, p. 284

34 Schaefer, S. Berl. klin. Wchnschr. 17 725, 1880

35 Noorden, C. Berl. klin. Wchnschr. 38 1057, 1901

36 Packard, F. A. Philadelphia M. J. 9 929, 1902

passage of gas by bowel within a very few hours of the completion of the operation Arndt,<sup>37</sup> in 1904, reported five cases in which the injection of physostigmine salicylate was apparently of life-saving value and stated that he had never seen this drug fail in the treatment of patients with ileus, except in cases due to acute bacterial peritonitis Vogel,<sup>38</sup> in 1904, reported favorable results following the routine injection of 0.0004 Gm of physostigmine given to patients soon after operation, during three years he saw no cases of ileus In cases of intestinal adhesions, he recommended the injection of physostigmine while the patient was still on the operating table He expressed the opinion that this method was of prophylactic value in the prevention of recurrent adhesions Craig,<sup>39</sup> in 1904 and 1905, warmly advocated the prophylactic use of physostigmine in the prevention of postoperative ileus, especially in the prevention of postoperative ileus due to adhesions Góth,<sup>40</sup> in 1908, reported the cases of three patients with ileus treated successfully by the administration of physostigmine at a time when they were apparently moribund Moenninghoff<sup>41</sup> warmly recommended the prophylactic use of physostigmine in the prophylaxis for distention following laparotomy He gave  $\frac{1}{40}$  grain (0.001 Gm) of the drug immediately following operation and followed this with an enema, because he believed that physostigmine acts only on the small bowel Martzloff,<sup>42</sup> in 1924, in a clinical report from the Johns Hopkins Hospital, said that he found the prophylactic administration of physostigmine salicylate in a dose of 0.01 Gm and strychnine sulphate in a dose of  $\frac{1}{40}$  grain (0.001 Gm) given hypodermically of little or no value in the prophylaxis of postoperative complications He reported the cases of 162 patients observed during a period of eleven months, all of whom had been subjected to major abdominal operations under ether anesthesia The series of cases is well controlled in that alternate cases received drug therapy He concluded that distention gas pains and emesis occur more frequently in patients treated thus than in a similar series of untreated patients Voluntary micturition was also established earlier in the nontreated than in the treated patients Martin and Weiss<sup>43</sup> reported favorably on the use of physostigmine in the treatment for abdominal distention Their clinical observations led them to believe

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37 Arndt Gustav *Zentralbl f Gynak* **28** 273, 1904

38 Vogel, K. *Zentralbl f Gynak* **28** 699, 1904

39 Craig, Daniel H. *Am J Obst* **49** 449 1904

40 Góth L. *Zentralbl f Gynak* **32** 1629 1908

41 Moenninghoff, F. I. *J Missouri M A* **5** 193, 1908

42 Martzloff K. H. *Bull Johns Hopkins Hosp* **35** 370 1924

43 Martin H. C. and Weiss S. *The Use of Physostigmine in Abdominal Distention* *J A M A* **84** 1407 (May 9) 1925

that the smallest single therapeutic dose that will afford relief is 2 mg, or  $\frac{1}{30}$  grain. The average dose which they employed was 4 mg, or  $\frac{1}{10}$  grain (0.004 Gm). As high as 13 mg, or  $\frac{1}{2}$  grain, was administered to one patient. They administer the drug by the intramuscular route, and in from ten to forty minutes after the injection they found that the patient belches or expels gas from the rectum. This effect gradually increases in frequency, and the volume of gas expelled also increases, defecation characteristically occurs, sometimes accompanied by moderate colic. In a total of sixteen cases of abdominal distention following laparotomies all of the patients were relieved from their symptoms by the injection of the drug. Vogel<sup>38</sup> recently, in 1928, reported good clinical results with the use of physostigmine.

*The Action of Choline and Acetyl Choline*—In 1912, Weiland<sup>44</sup> made the accidental observation that when isolated strips of intestine were allowed to contract for considerable periods of time in Ringer's solution, the Ringer's solution when brought into contact with other pieces of intestine showed the property of producing excitation in them. The substance responsible for this reaction was isolated first in Magnus's laboratory at Utrecht, by LeHeux.<sup>29</sup> Magnus<sup>45</sup> thought that he had isolated the hormone responsible for the regulation of intestinal activity, since it was found not to affect the uterus or heart but was specific for the intestinal musculature. This substance called choline, is apparently derived from the intestinal musculature itself, and the intestine has been found to conserve its supply of the material. The first experiments with choline were performed in Magnus's laboratory, and it was found by fluoroscopic examination that paralysis of the intestine induced by prolonged chloroform narcosis was speedily relieved by the injection of from 5 to 15 mg of choline per kilogram of body weight. Magnus<sup>45</sup> determined the safe intravenous dose in cats as 20 mg of the substance per kilogram of body weight, and he found that when injected at a rate of 0.8 mg per kilogram per minute large doses of the drug were tolerated. Holt and Grossman<sup>46</sup> stated that choline is normally present in the musculature of the stomach and the intestine. They said that the substance is not absent from the gut in ileus. Magnus,<sup>45</sup> in 1925, stated that choline activates the plexus of Auerbach, since, if the plexus is removed, much larger doses of choline are required to stimulate the muscle. He stated that the isolated small intestine of the rabbit gives off 3 mg of choline from its serosal side during the course of an hour. This author<sup>45</sup> is authority for the statement that the choline content is almost invariably found to be normal in all cases save in morphine poisoning.

44 Weiland, W. *Verhandl. d. Kongr. f. inn. Med.* **29** 165, 1912.

45 Magnus, R. *Munchen med. Wchnschr.* **72** 249, 1925.

46 Holt and Grossman. *Munchen med. Wchnschr.* **72** 251, 1925.

Guggenheim and Loeffler<sup>47</sup> made quantitative analyses of the amount of choline in the blood and urine. They found that a liter of urine contained from 0.002 to 0.01 Gm of choline hydrochloride, and that a liter of serum contained from 0.002 to 0.02 Gm. Choline has the formula *trinethyloxyethylammonium hydrochloride*. Dale,<sup>48</sup> in 1914, investigated the action of four different esters of choline: (1) the choline nitrous ester, the so-called synthetic muscarine of Schmiedeberg and Harnach, (2) the choline nitric ester, (3) the choline ethyl ether, and (4) acetyl choline. All four substances were found to be powerful stimulants to the musculature of the esophagus and stomach and to the small and large gut. In the intact animal, acetyl choline was found to be the weakest of the four drugs when injected intravenously, the other esters showed more powerful and prolonged action. On the isolated muscle, however, acetyl choline was somewhat more active than the other three. The explanation offered for this observation is that acetyl choline is very rapidly oxidized in an alkaline medium, the drug, when injected intravenously, reaches the heart relatively rapidly and affects it maximally, but it reaches the intestine only after considerable time has elapsed, during which oxidation has occurred. Dale<sup>48</sup> found that 0.000001 mg of acetyl choline produced a definite decrease in the blood pressure of the cat. LeHeux<sup>49</sup> isolated acetyl choline, as well as choline, and acetyl choline was found to produce a reaction of the order of a hundred times as great as choline alone. LeHeux<sup>49</sup> working in 1921 and experimenting on the choline esters of succinic, pyruvic, butyric, isovaleric and benzoic acids, found that the succinic ester of choline showed no greater effect than did choline alone. He gave the relative value of the various other esters as follows: The choline ester of acetic acid is 1,000 times as powerful an intestinal stimulant as choline itself, propionic acid, 300 times, formic acid 100 times, butyric acid, 40 times, isovaleric acid, 15 times, and benzoic acid, twice.

Most authors accept the statement that acetyl choline is 1,000 times as powerful an intestinal stimulant as is choline, e. g. Wolf and Canney<sup>49</sup> and Magnus<sup>50</sup>.

Wolf and Canney<sup>49</sup> reported the effect of the injection of choline in four clinical cases, in three of which the injection was believed to have been of life-saving value. Arai<sup>50</sup> was able to relieve experimentally produced ileus in cats by the use of choline, ileus having been produced (1) by intraperitoneal injections of iodine, (2) by laparotomy and trauma to the intestine and (3) by the production of an infective peri-

47 Guggenheim M and Loeffler W. *Biochem Ztschr* **74** 208 1916

48 Dale, H H. *J Pharmacol & Exper Therap* **6** 147 1914-1915

49 Wolf C G L, and Canney J R C. *Lancet* **1** 707, 1926

50 Arai K. *Arch f d ges Physiol* **193** 359 1922

tonitis Klee and Grossmann<sup>51</sup> reported that they had given choline intravenously in 120 cases, only a few of which, however, have been cases of ileus. They used pure choline hydrochloride, one ampule of which contained 0.6 Gm. of the drug. They added the drug to 240 cc. of sterile warm saline solution and introduced the solution into a vein slowly by gravity. Holt and Grossman<sup>46</sup> advocated a dose for man of 600 mg. per kilogram of body weight, given over a period of seventeen minutes, favorable case reports are included. Magnus,<sup>45</sup> in 1925, advised a dose of 10 mg. of choline per kilogram of body weight in man. This dose, he said, should not be given faster than 0.6 mg. per kilogram per minute, the injection of such a dose occupies seventeen minutes. Carlson, Smith and Gibbens<sup>52</sup> attempted to determine the action of choline on the alimentary tract of intact dogs. Using barbitol anesthesia, introducing rubber balloons into various parts of the gastro-intestinal tract, thereafter closing the abdomen with as little trauma as possible, and recording movements of the intestine by means of a water manometer, they found the effect of choline on the motor phenomena variable consisting of (1) pure inhibition of tonus and motility, (2) inhibition of tonus and motility followed by a period of increased tone and (3) a rather exceptional observation, increased tonus and motility without inhibition. The small intestine was found to be most sensitive to the action of choline, it characteristically showed inhibition of tone and motility, followed by increased tone, sometimes pure inhibition or pure augmentation of tone was noted. The stomach was found usually to be insensitive to small doses but when larger doses were given it usually showed late and temporary increases of tone. The transverse portion of the large intestine usually exhibited depressions of tone and motility but occasionally showed slight increase of tone. LeHeux,<sup>49</sup> by means of roentgenographic studies, was able to demonstrate that the administration of choline stimulated the movements of the stomach and small intestines and hastened the passage of intestinal contents through the lumen of the large bowel. Von Kuhlewein<sup>53</sup> found by fluoroscopic studies that chloroform anesthesia produced, within a period of two hours, an ileus that lasted for twenty minutes. This variety of ileus was relieved to a large extent by the injection of from 0.005 to 0.15 Gm. of choline hydrochloride per kilogram of body weight. Immediately after the administration of this dose of choline definite evidences of peristalsis could be seen. Guggenheim and Loeffler<sup>47</sup> expressed the belief that the activating substance in intestinal movement is in reality not choline but acetyl choline. Brunner and Weigand<sup>10</sup> expressed the belief that acetyl choline should not be used

51 Klee, P., and Grossmann, O. *Munchen med Wchnschr* **72** 251, 1925

52 Carlson, A. I., Smith, E. A. and Gibbens, I. *Am J Physiol* **81** 431 1927

53 von Kuhlewein, M. *Arch f d ges Physiol* **191** 99 1921

clinically for the relief of ileus because of the danger of unfavorable associated actions of the drug

*The Action of Hypertonic Sodium Chloride Solutions*—Ross<sup>54</sup> in 1926, in experimental animals using a rubber balloon introduced into the normal intestinal canal and connected by means of rubber tubing to a manometer, showed that following the injection of a 30 per cent solution of sodium chloride in a dose from 0.33 to 0.166 Gm per kilogram of body weight, there was an immediate increase in tone followed by marked peristalsis. Injection of sodium chloride in this manner succeeded in producing effects in cases in which both physostigmine and pituitary extract had failed to produce any response. He reported three clinical cases in which the intravenous injection of hypertonic salt solution was successful in overcoming ileus after all other measures had failed. Coleman<sup>55</sup> in 1927, working on the basis of Orr's suggestion that 3 per cent sodium chloride solution can be used in cases of ileus to combat intestinal paralysis, reported thirty-eight clinical cases occurring over a period of six years, from January 1921 to December, 1926. The cases are divided into two groups. In the first series in which saline solution was not used they reported twenty cases of ileus with ten deaths a mortality of 50 per cent. In a second series of cases, numbering eighteen, making use of 3 per cent sodium chloride, they reported only two deaths or 11.1 per cent. They admitted that the series of cases was small but they expressed the opinion that the two series are comparable and that the decreased mortality in the second group of cases is due entirely to the use of the 3 per cent sodium chloride solution. McIntosh and Owings<sup>56</sup> using a special technic for recording increases of intestinal pressure in animals found that concentrated solutions of sodium chloride were capable of increasing the intra-intestinal pressure. Rame and Perry<sup>57</sup> using rabbits and employing a special technic for the recording of intra-intestinal pressure found that in obstructed animals the intravenous administration of 5 per cent sodium chloride stimulated peristalsis sufficiently to cause propulsion of the intestinal contents and give relief from increased intra-intestinal pressure.

#### REPORT OF EXPERIMENTAL RESULTS

*Preliminary Note*—The experimental results to be reported are presented in as objective terms as possible. The figures for blood pressure are subsequently given and represent absolute values as recorded by the mercury manometer. Increases in intestinal tone and movement are reported also in terms of figures. These figures how-

<sup>54</sup> Coleman E. P. *Anesth. & Analg.* 6:210, 1927.

<sup>55</sup> Rame F. and Perry M. C. *Intestinal Obstruction*. *Arch. Surg.* 19:478 (Sept.) 1929.

ever, represent no absolute values, but rather millimeters of excursion of the recording point on the kymographic drum. As the excursion of such a recording lever depends not only on the amount of movement in the intestine but also on variable mechanical factors, such as the length of the lever and the distance of the fulcrum from the point of application of force, these figures are of only relative significance. However, as the physical disposition of apparatus was not changed during the entire course of the experiments reported in this communication, the figures given are directly comparable, and the amount of absolute movement of the writing point becomes of comparatively little importance.

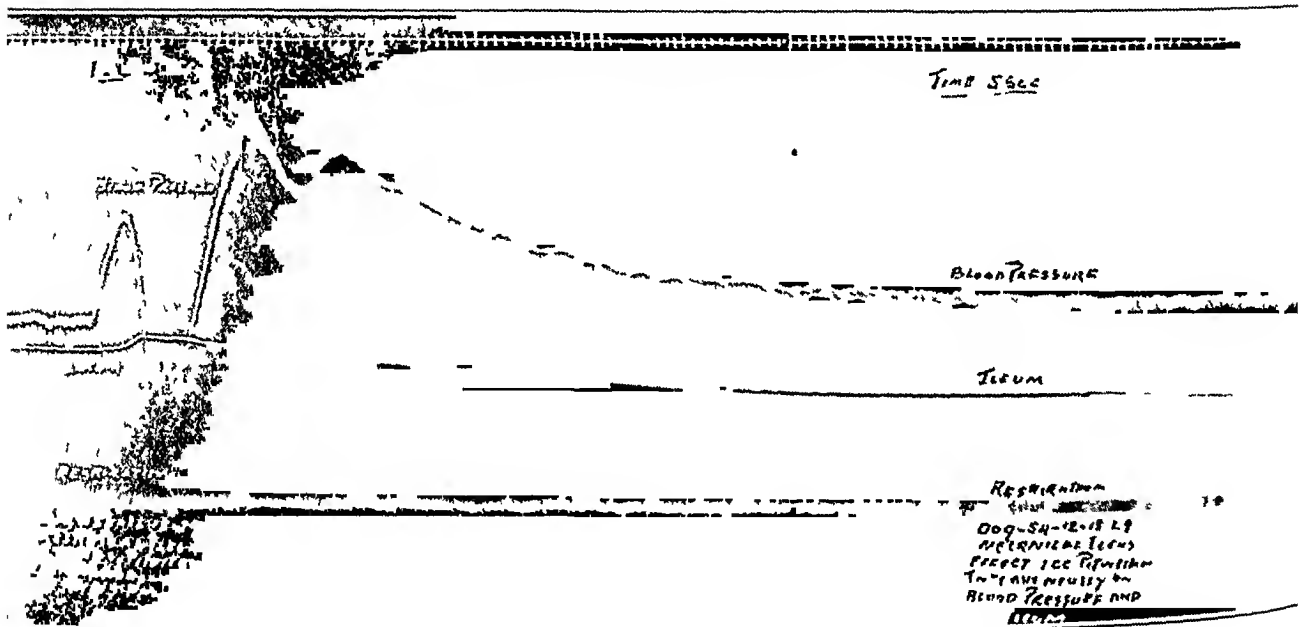


Fig 1—Kymographic tracing, showing the effect of the injection of 1 cc of obstetrical pituitary extract into an animal with an artificial obstruction of forty-eight hours' duration. The effect on the blood pressure is typical. There is an initial phase of increased blood pressure, a second phase of decreased blood pressure to a low level and a third phase of increase of blood pressure to a new high level, followed by a progressive and prolonged decrease to normal. The effect on the ileum is somewhat atypical in that a slight preliminary increase in tone is noted, but this is transient and is followed by a typical effect, namely, a progressive decrease in tone and absence of stimulation of motor activity.

*The Effect of Pituitary Extract*—The effect of the intravenous or intramuscular injection of 1 cc of pituitary extract was observed twenty-nine times in twenty-four animals. Twenty of these observations were made on normal animals and nine in animals with a forty-eight hour old mechanical obstruction.

The effect of pituitary extract in the case of normal animals was as follows:

(a) On the Blood Pressure The characteristic effect of the injection of pituitary extract on the blood pressure consisted of three phases (1) a transitory increase, which was moderate in degree, (2) a subsequent depression to a value below normal and (3) a subsequent increase soon thereafter to a level much greater than before. After this the effect tended to be persistent or to subside, the blood pressure being maintained for many minutes thereafter at a relatively high level or

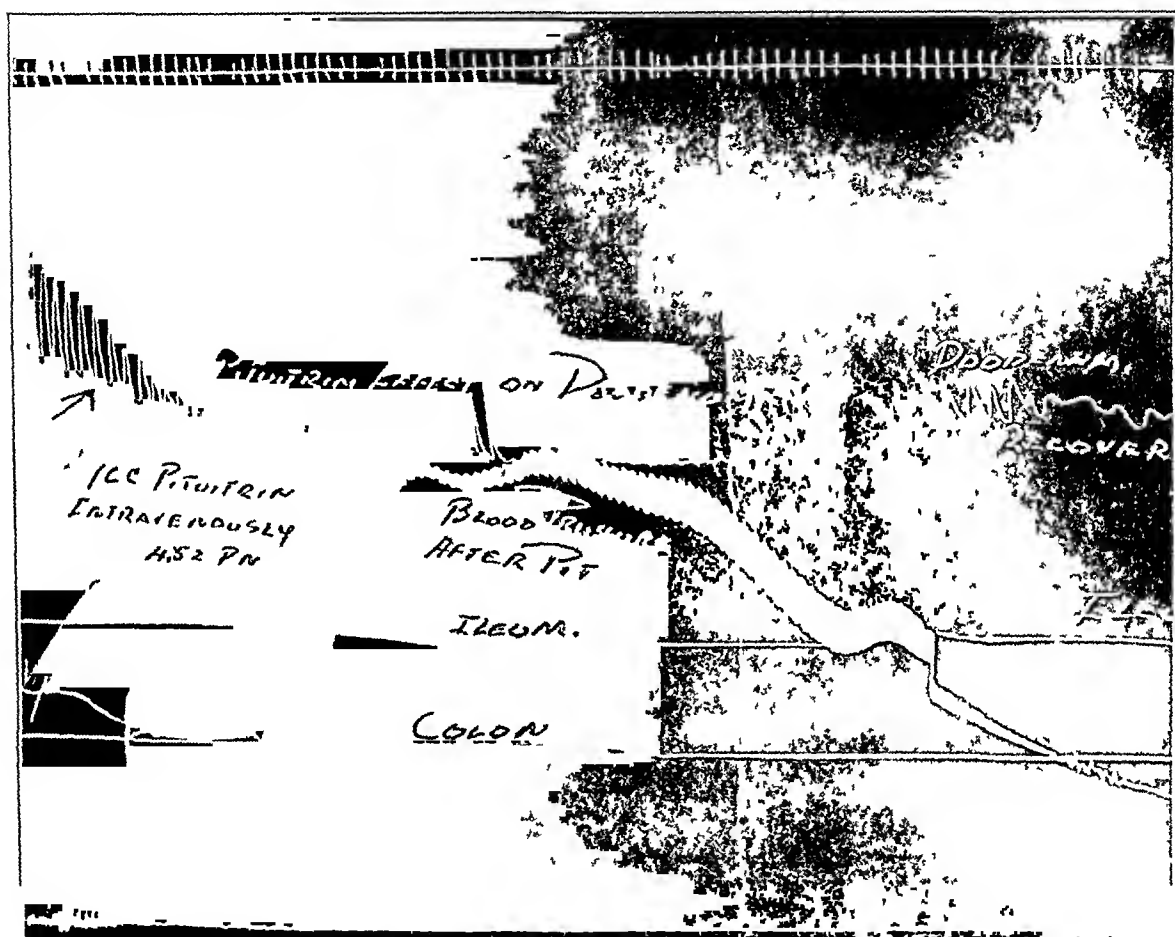


Fig 2—Kymographic tracing showing the effect of the intravenous injection of 1 cc of pituitary extract on the blood pressure duodenum, ileum and colon. Within about a minute the blood pressure shows a marked increase which is sustained with slight variations for a period of about two minutes after which it progressively decreases during a period of about three minutes to a point below the normal level. Within a minute duodenal movement which previous to the injection had been considerable, was reduced almost to the vanishing point, and a moderate decrease in intestinal tone occurred. In about five minutes duodenal movements began to be reestablished. The effects on the ileum and colon are slight. There is possibly a slight decrease in tone in both ileum and colon.

a gradual decrease in pressure then occurring for a similar period of time (fig 1). Although this was the effect characteristically seen variations were not infrequently encountered. In fact in certain rare



cases injection of the drug produced a simple depression in the blood pressure. In seventeen of the twenty observations the first phase of initial rise in blood pressure, as previously described, was encountered. This occurred in from one to five minutes, and the average increase in blood pressure encountered was 37 mm of mercury. In two cases during a comparable initial period there was no change in the blood pressure, and in one case a slight depression was encountered. In the succeeding period of from one to five minutes, the blood pressure showed the characteristic secondary decrease in six of the observations. The average decrease was 32.5 mm of mercury, the initial normal blood pressure of the animal being taken as a standard. In seven

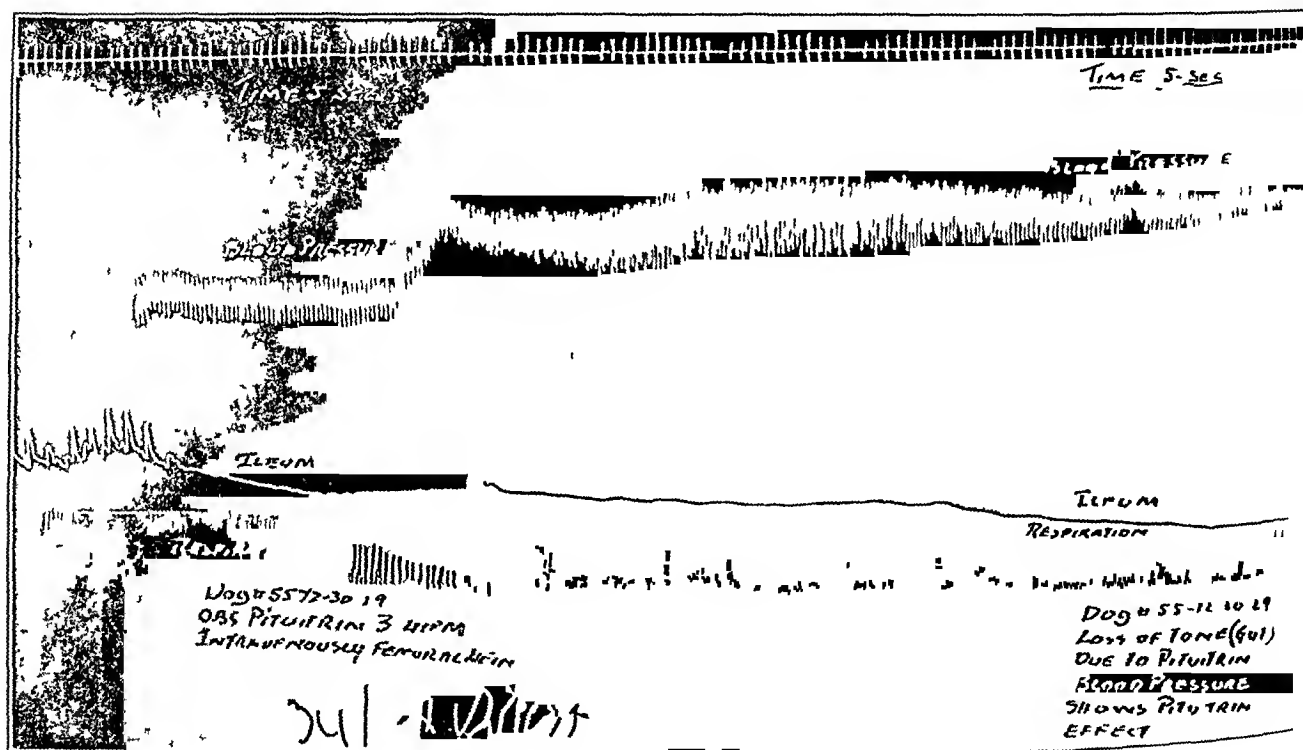


Fig 3—Kymographic tracing, showing the effect of 1 cc of pituitary extract on the blood pressure and on the ileum. In this case about two minutes after the injection of pituitary extract the blood pressure increased rather abruptly and remained for at least ten minutes at a somewhat elevated level. Within one minute movement in the ileum, which previously had been considerable, ceased almost completely, and a decrease in intestinal tone occurred which persisted for at least ten minutes.

cases in the second phase the blood pressure showed no decrease but remained sustained. In the other cases (namely, seven) variations of blood pressure during the second phase interfered with the interpretation of the results obtained. In the third phase of the reaction four of the animals showed still further increases in the blood pressure, the average increase being 31 mm of mercury. Animals that previously had

shown a sustained effect during the second phase continued to show this effect, and in the animals that had shown no distinct change in the second phase no characteristic effect was seen in the third stage

(b) On the Intestine The characteristic effect of pituitary extract on the intestine was one of decrease in tone and inhibition and peristaltic movement. There were however a few notable exceptions to this rule. Quoting figures from the statistical study decrease in tone was noted in sixteen of the twenty cases, no change of tone was encountered in two cases and in two cases actual increases of tone occurred. The average decrease in tone in all cases in which the decrease

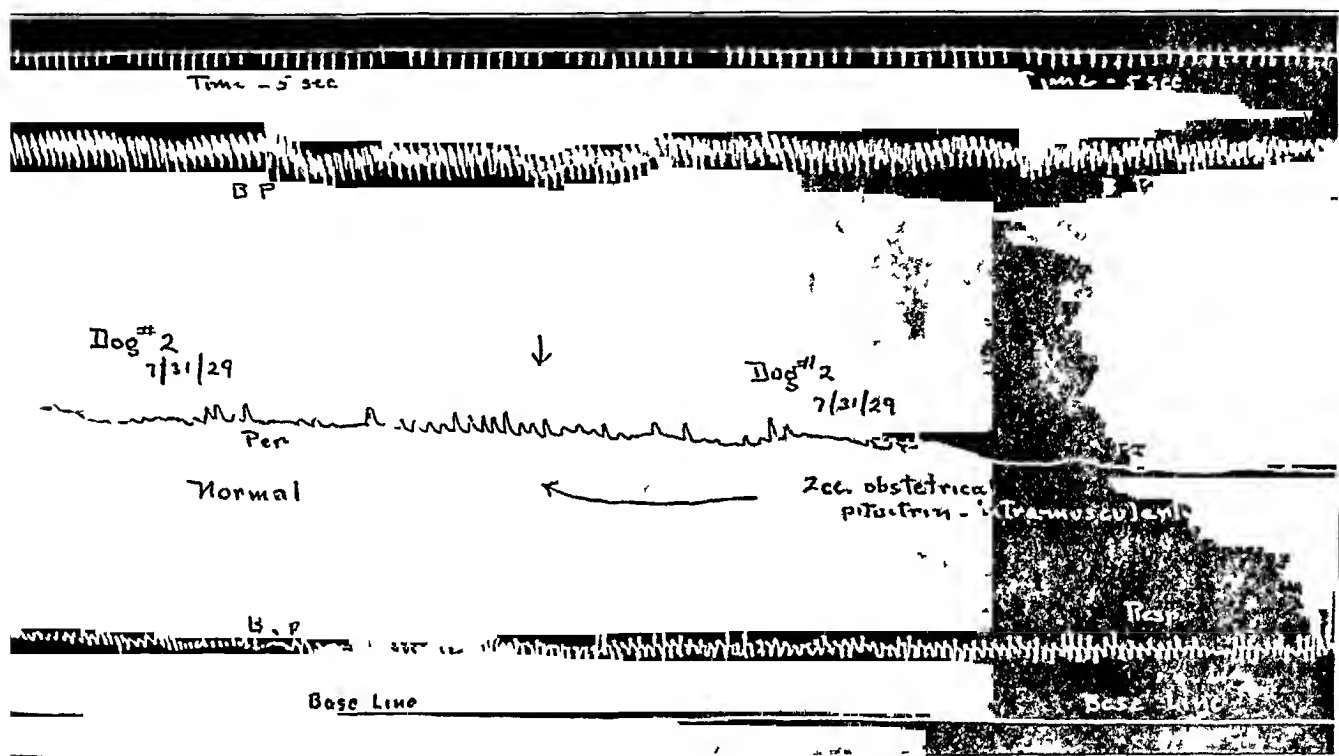


Fig 4—Kymographic tracing showing the effect of the injection of 2 cc of obstetrical pituitary extract intramuscularly. No noticeable effect on the blood pressure is seen. The effect on the ileum is characteristic. Within two and one-half minutes, intestinal movement, which previously had been rather active subsided and moderate decrease in intestinal tone ensued.

could be measured was 75 mm. In the two cases that showed increases of tone (10 per cent of the cases) the effect was pronounced the average increase being 26 mm.

In 75 per cent of the cases (fifteen cases) the amplitude of intestinal movement either remained as before the injection (five cases 25 per cent) or decreased somewhat. The average decrease was 32 mm. In 25 per cent of the cases that is in five cases injection of the drug resulted in increased amplitude of intestinal movement averaging 5 mm.

(c) Effect on Respiration No constant effect was noted on the respirations of the animals used. In nine cases interpretation of the respiratory tracing was not clear. In five of the remaining cases the injection of pituitary extract produced no effect, and in five it produced a moderate decrease in respiratory excursion.

The effect of pituitary extract on animals with obstruction was as follows:

(a) Effect on the Blood Pressure On the blood pressure the injection of pituitary extract invariably (except one case) produced

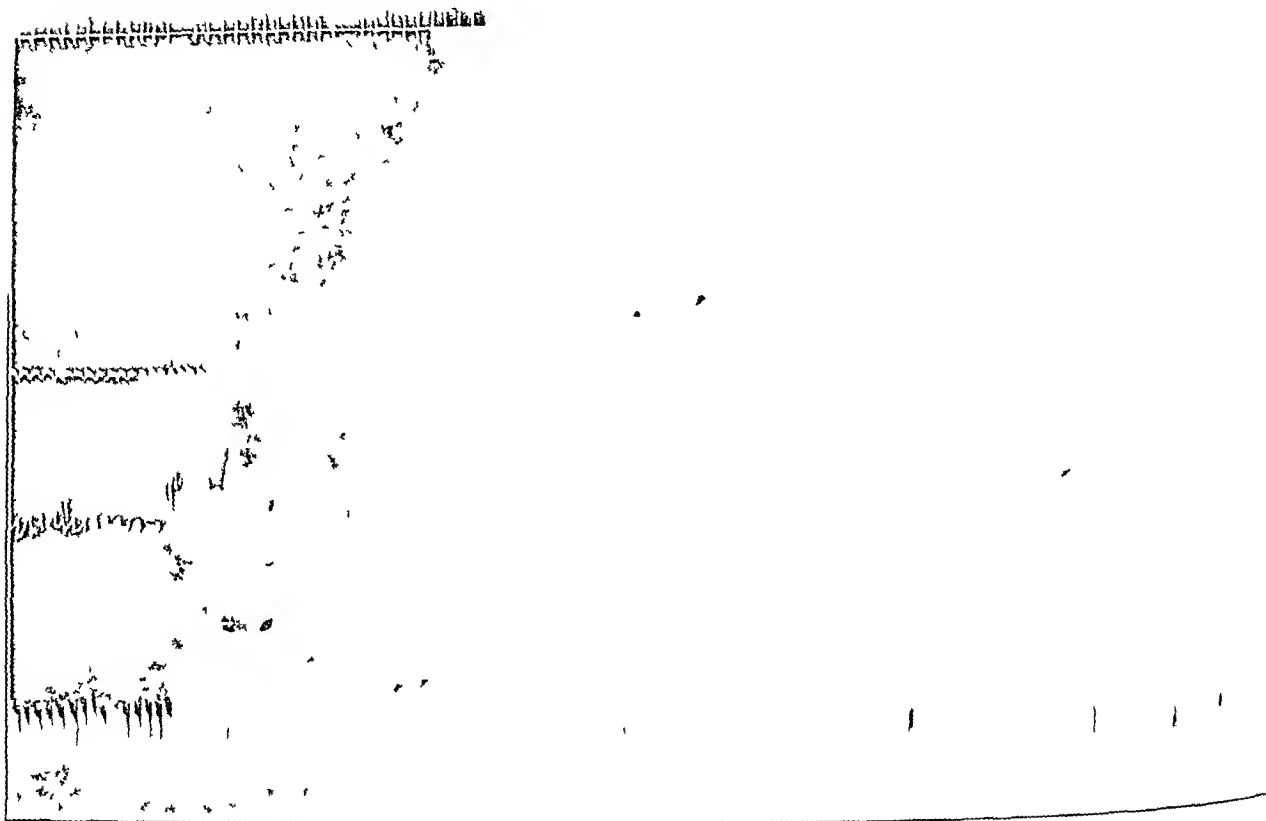


Fig 5—Kymographic tracing, showing the effect of the intramuscular injection of 1 cc of obstetrical pituitary extract. In this case relatively little effect on the blood pressure is seen, although a transitory (two minutes) slight increase in the blood pressure may have been due to the effect of the drug. After five minutes, intestinal motility in the ileum, which previously had been active, subsided and a progressive decrease in tone ensued. The latent period in this case is rather long but the pituitary extract was injected intramuscularly, and this may account for the retardation of the effect.

an initial phase of temporary increase which occurred in from one-half to three minutes. The average increase during this phase was 41.8 mm of mercury. In the second phase, within one-half minute or longer, the blood pressure decreased on an average of 56 mm in five of the nine cases. A third phase occurred in four of the animals within a

minute or two consisting of an increase of blood pressure averaging 56.5 mm. In one of the nine animals the blood pressure showed no noticeable effect. In one case the initial rise of blood pressure was sustained at an increased level of 35 mm of mercury. In two cases the initial rise in blood pressure was immediately followed by a progressive decrease.

(b) Effect on the Intestines. In six of the nine animals noticeable decreases in intestinal tone followed the injection of pituitary extract. In four animals the average decrease in tone was 9.2 mm. The other two animals showed unmeasured decreases. Only one animal showed

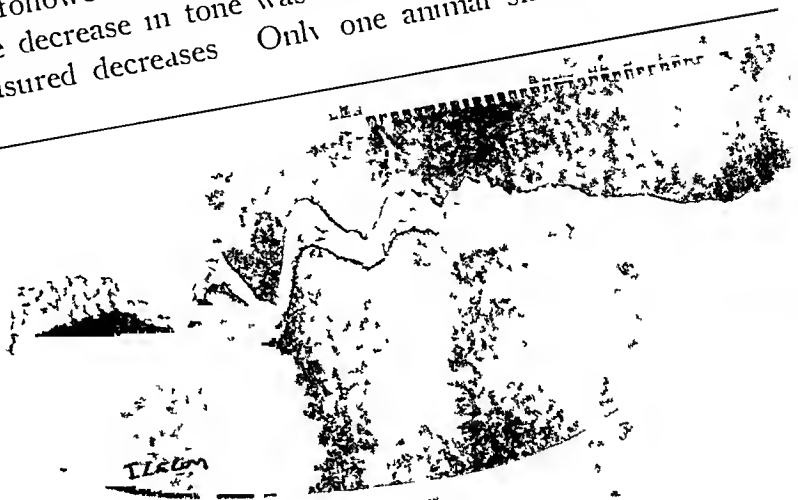


Fig 6—Kymographic tracing showing the effect of the intravenous injection of 1 cc of obstetrical pituitary extract. The effect on the blood pressure is typical showing an initial increase, a second phase of decrease and a third phase of increase to a new high level. In this instance the high blood pressure level was maintained for a considerable period of time. The effect on the intestine was somewhat atypical, showing a preliminary decrease in tone followed by a marked and more or less prolonged increase in tone. Complete cessation of intestinal movement was seen, although the normal movement in the ileum in this case was only slight.

an increase in tone. This was considerable (50 mm) but was temporary, lasting only a minute. In none of the animals was the amplitude of intestinal movement increased. One animal showed a reduction in amplitude of 20.5 mm, two animals showed a decrease which was just appreciable (1 mm) and in the remaining animals the amplitude of movement was unaffected.

(c) Effect on Respiration The effect on respiration seen in these animals was virtually nil. In three cases, however, the respiratory amplitude seemed to be somewhat decreased.

(d) Comparison of the Effect of Pituitary Extract in Normal Animals and in Animals with Obstructed Guts The series of animals subjected to the injection of pituitary extract is admittedly small. The effect on the obstructed gut is similar to that on the normal gut, and any statement further than this would seem to be unjustified in the light of the relatively inconsiderable number of animals used and the considerable number of variations noted.

Exceptionally, pituitary extract seems to be capable of producing decided increases in tone in the intestinal musculature. In paralytic ileus such increases in tone, so far as we have been able to observe, are of much greater value in extruding material from the gut than increases

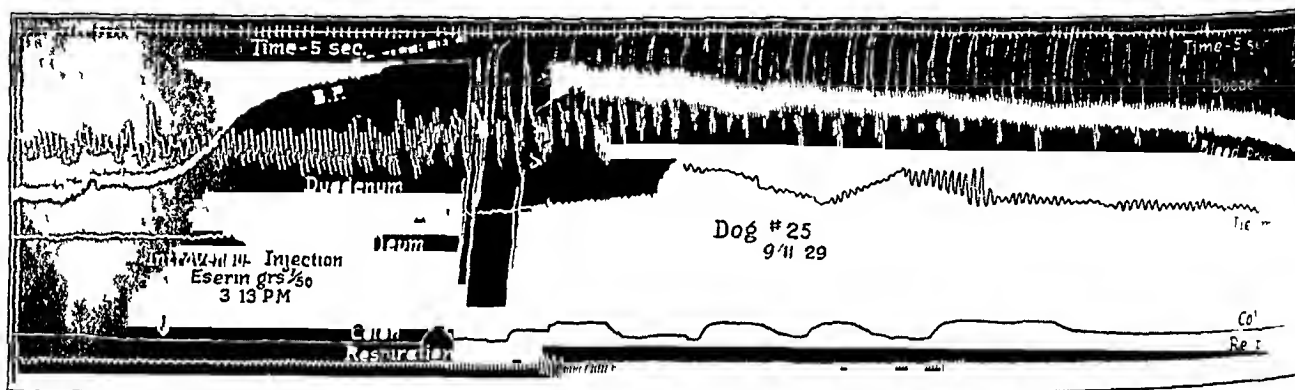


Fig 7—Kymographic tracing, showing the effect of the intravenous injection of  $\frac{1}{50}$  gram of physostigmine into a normal animal. In this tracing duodenal, ileal and colonic tracings were recorded simultaneously. The effect on the blood pressure is typical, showing a considerable, slow increase in blood pressure followed by a prolonged and progressive decrease. The effect on the duodenum is a very decided and prolonged increase in the amplitude of intestinal movement, accompanied by a slight increase in tone. The effect on the ileum is typical—a slow progressive increase in tone with the ultimate production of a rather marked increase in the amplitude of intestinal movement. The effect on the colon is one of increased movement, but the tone itself remains relatively unchanged.

in intestinal motility. The reason for this is fairly obvious. The contents of the gut characteristically consist of fluid material and gas. Intestinal movements alone may merely mix such contents without propelling them, peristaltic waves passing the length of the gut, but the contained fluid and gas regurgitating through the advancing ring of peristaltic constriction as soon as any considerable increase in intra-intestinal pressure is produced ahead of the peristaltic wave. If pituitary extract would always increase intestinal tone as it does in the exceptional case it would be of considerable value. Apparently, those who

have reported favorably on the clinical use of pituitary extract have been fortunate enough to encounter the exceptional action of the drug

*The Effect of Physostigmine*—Physostigmine in the form of physostigmine sulphate was injected twenty-four times into twenty-one dogs. The dose of the drug was  $\frac{1}{50}$  grain (0.0013 Gm.) injected intravenously. Ten of the observations were on animals that had undergone experimental mechanical obstruction forty-eight hours previously. The other fifteen observations were on normal animals.

The effect of physostigmine on normal animals was as follows:

(a) *The Effect on Blood Pressure* In every case except one the blood pressure increased, following the injection of physostigmine. The amount in every case was significant. The single case in which no increase was noted showed a decrease of 20 mm. of mercury. Earlier

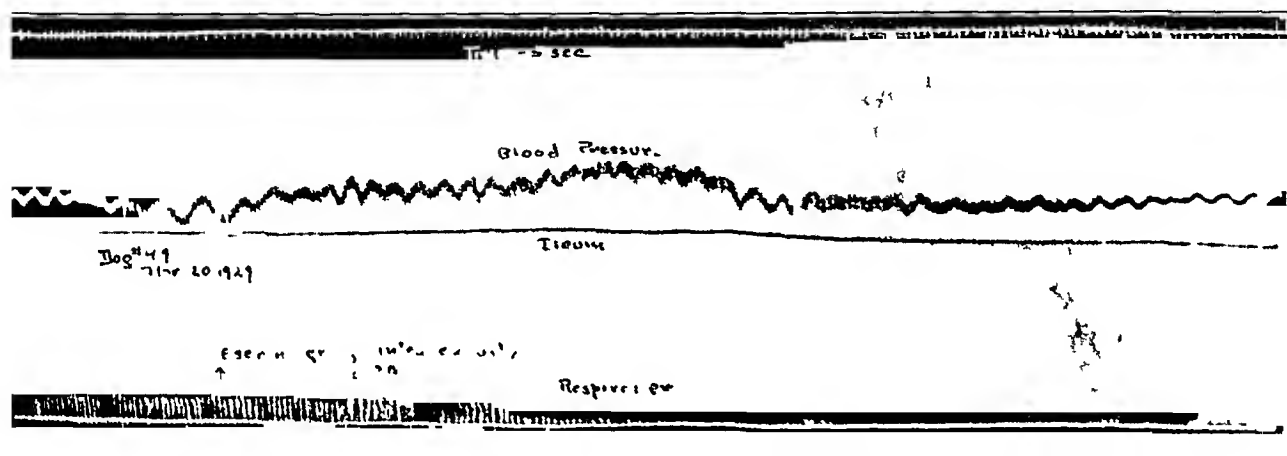


Fig. 8—Kymographic tracing showing the effect of the injection of  $\frac{1}{50}$  grain of physostigmine intravenously into a normal dog. The effect on the blood pressure is typical and consists of an irregular, gradual increase in blood pressure. The effect on the ileum in this case is virtually nil. However, on close inspection, variations in tone can be appreciated.

in the afternoon in which the experiment was performed this animal had received a prior injection of the same drug. The average increase in blood pressure shown by the other animals was 17.2 mm. The average duration of the rise of blood pressure caused by the injection was three and eight-tenths minutes. In all cases the blood pressure returned either to a normal or to a subnormal level and the average duration of the decrease to a normal level was twelve and seven-tenths minutes. In two of the seventeen cases the blood pressure eventually fell to a level of 20 mm. below that seen at the time of injection.

(b) *Effect on the Intestines* With the exception of one instance the tone of the intestine invariably rose as the result of the injection of physostigmine. In the atypical case there was a decrease of 10 mm. in tone which lasted for twenty minutes. The average increase in

tone in the fourteen cases in which this effect was seen was 26 mm, and the average latent period between the time of injection and the beginning of the effect on tonus was four minutes. The injection of physostigmine characteristically produced augmentation of the intestinal movement. The average increase in amplitude of these movements was 3.9 mm, and "tonus waves" were apparently produced by the drug in two instances. Atypical effects on intestinal movement were seen in two instances. In these two cases there was no increase in movement. The drug simply showed failure to produce a typical augmentation.

(c) *Effect on Respiration* The effect on respiration was inconstant. The amplitude of respiration was apparently decreased in four cases, increased in one case and showed no effect in the others.

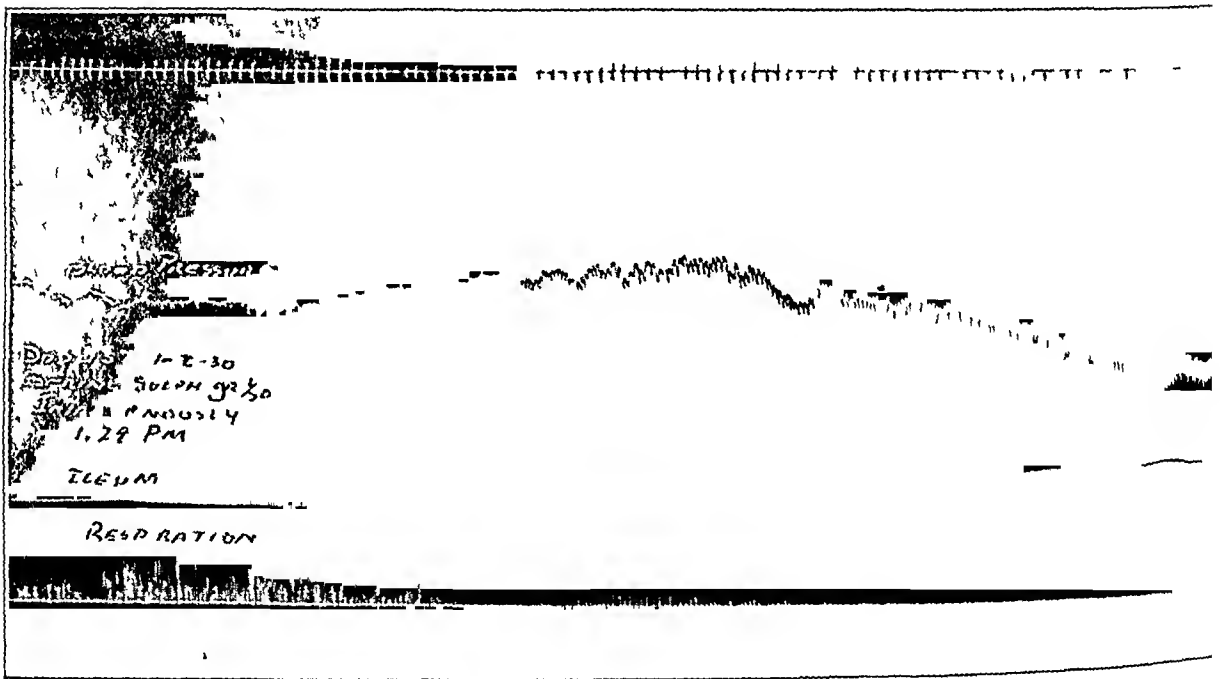


Fig 9—Kymographic tracing, showing the effect of the injection of  $\frac{1}{50}$  gram of physostigmine sulphate intravenously into a normal dog. The initial effect on the blood pressure is typical, showing a moderate increase. The progressive decrease, however, which characteristically follows, is exaggerated in this case, and the blood pressure actually decreases to a new low level. The effect on the ileum is typical in that the tone shows a gradual increase, and definite, though slight, intestinal movement is initiated.

The effect of physostigmine on animals with obstructed guts was as follows:

(a) *Effect on Blood Pressure* In all but two cases the effect of the injection of physostigmine was to increase the blood pressure. The average increase in the thirteen cases showing this typical effect was 32 mm of mercury; the average latent period between the injection of the drug and the beginning of effect on blood pressure was four and three-tenths minutes. The other two cases showed an insignificant

decrease in blood pressure, the average being 3 mm. The average latent period of this reaction was six minutes.

(b) Effect on the Intestine. The characteristic effect of physostigmine was to increase both the tone of the intestine and the amplitude of its contractions.

(c) Effect on Tone. In eight cases there was an average increase in tone of 10.7 mm., but in one case the tone subsequently fell to a subnormal level. The average latent period between the injection of the drug and the beginning of the effect on tone was nine and two-tenths minutes. In three cases the tone of the intestine was unaffected; in four cases the tone actually fell, but the average decrease in these four cases was only 4 mm., the decrease in tone in the latter cases being only relatively slight and being gradual, could not be determined with

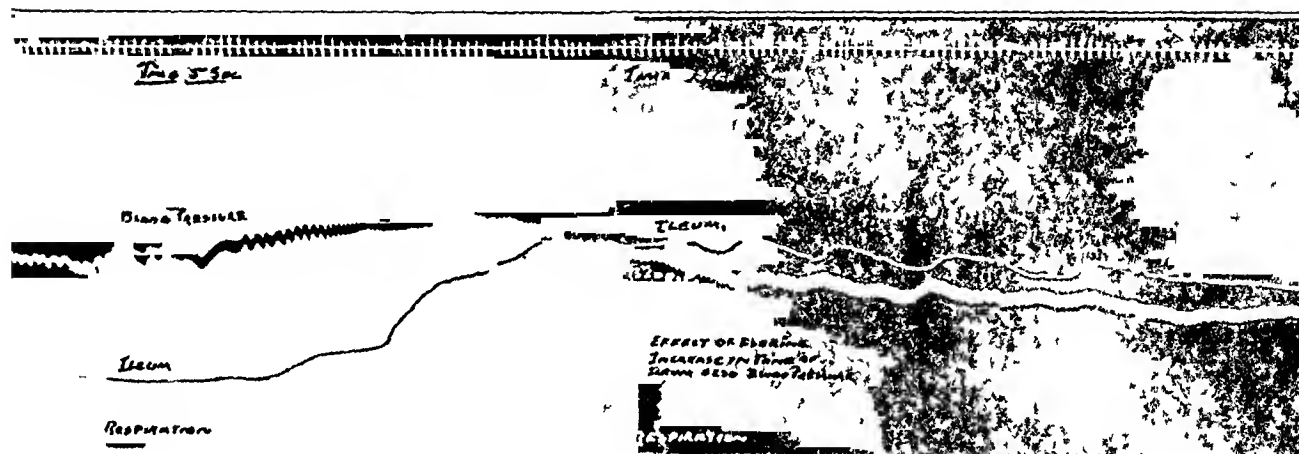


Fig 10—Kymographic tracing, showing the effect of the injection of 1.50 gram of physostigmine sulphate intravenously into a dog with mechanical ileus. The effect on the blood pressure is characteristic. A gradual initial rise in blood pressure was followed by a progressive decrease to a normal or even a subnormal level. The effect on the ileum is characteristic, but shows a rather exaggerated increase in tone and the ultimate development of tonus waves superimposed on which is evidence of slight intestinal movement.

accuracy. The effect of physostigmine on intestinal motility was not constant, but was decidedly in the direction of increased movement. A definite increase was noted in seven cases, the average increase in amplitude being 3.8 mm. In six cases intestinal movement was unaffected. In two cases the movement of the intestine was decreased, the average amount being 3 mm.

(d) Effect on Respiration. The effect of physostigmine on respiration was found to be negligible.

(e) Comparison of the Effect of Physostigmine in Normal Animals and in Animals with Obstruction. A consideration of the figures pre-



sented would seem to indicate that the effect of physostigmine on the animal with an obstructed gut is more consistent and profound than the effect on normal animals. Increases in intestinal tone were noted in only slightly more than one half of the normal animals, whereas 90 per cent of those with obstruction showed this effect. A similar effect was noted on the amplitude of intestinal movement, whereas the amplitude was increased in less than half the normal cases, 80 per cent of the cases that had undergone previous intestinal obstruction showed definite augmentation. The effect on blood pressure in the two series was reversed in that injection of physostigmine produced an average increase in blood pressure nearly twice as great in normal animals as in those with obstruction.

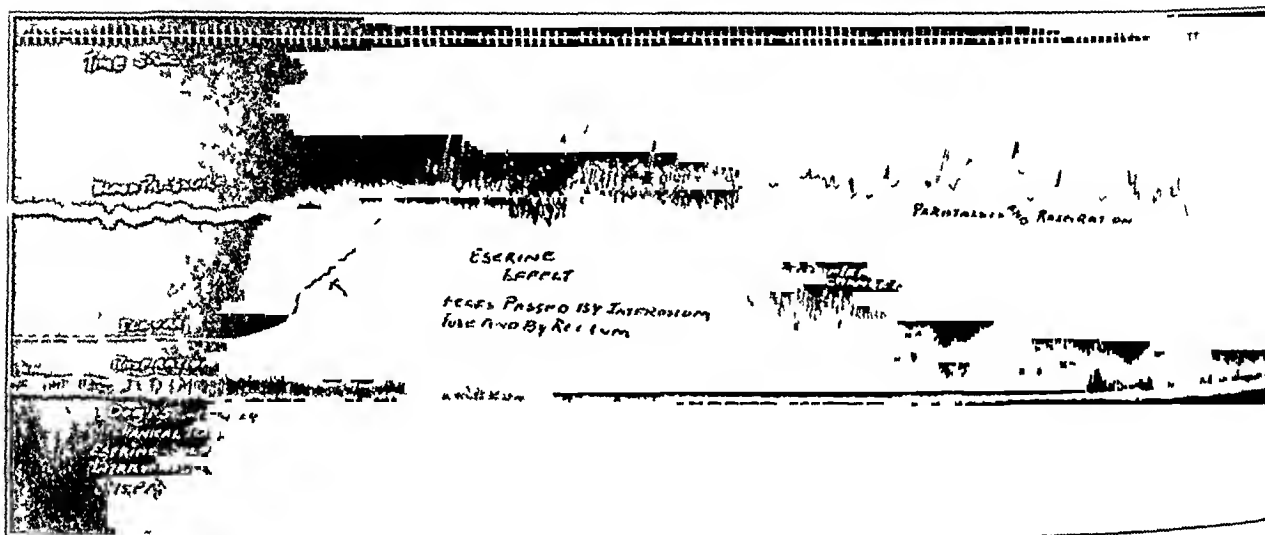


Fig 11—Kymographic tracing, showing the effect of the intravenous injection of  $\frac{1}{10}$  grain of physostigmine sulphate into a dog in which artificial mechanical ileus had been produced forty-eight hours previously. The effect on the blood pressure is somewhat atypical in that no significant increase in blood pressure is evident. The interruption in the blood pressure tracing, which occurs about the middle of the graph is not significant, since a mechanical readjustment of the writing point was made at this time. The effect on the ileum is typical but greater than that ordinarily seen. There is a rather sharp, progressive increase in tone followed by a decided increase in the amplitude of intestinal movement. Toward the end of the tracing certain of the irregularities which can be seen probably represent respiratory components, pressure changes being transmitted from the diaphragm to the intestine. The writing point of the blood pressure apparatus was depressed in order to make this part of the tracing visible.

*The Effect of Choline*—Choline was administered four times to four normal animals. A pure preparation of choline hydrochloride was used and this was dissolved in 100 cc of physiologic solution of sodium chloride. The solution containing the drug was injected into the vein of the animal by gravity and it was allowed to run only very slowly.

(a) Effect on Blood Pressure In three of the four animals the injection of choline was followed by rather rapid decreases in the blood pressure. Since the decreases in the blood pressure were directly proportionate to the rapidity with which the solution was introduced, the amount of blood pressure decrease is of little significance. The average was 13.3 mm. In one animal the blood pressure showed an increase of 10 mm. This increase in blood pressure was attributed not to the drug itself, but rather to the effect of the sodium chloride solution which

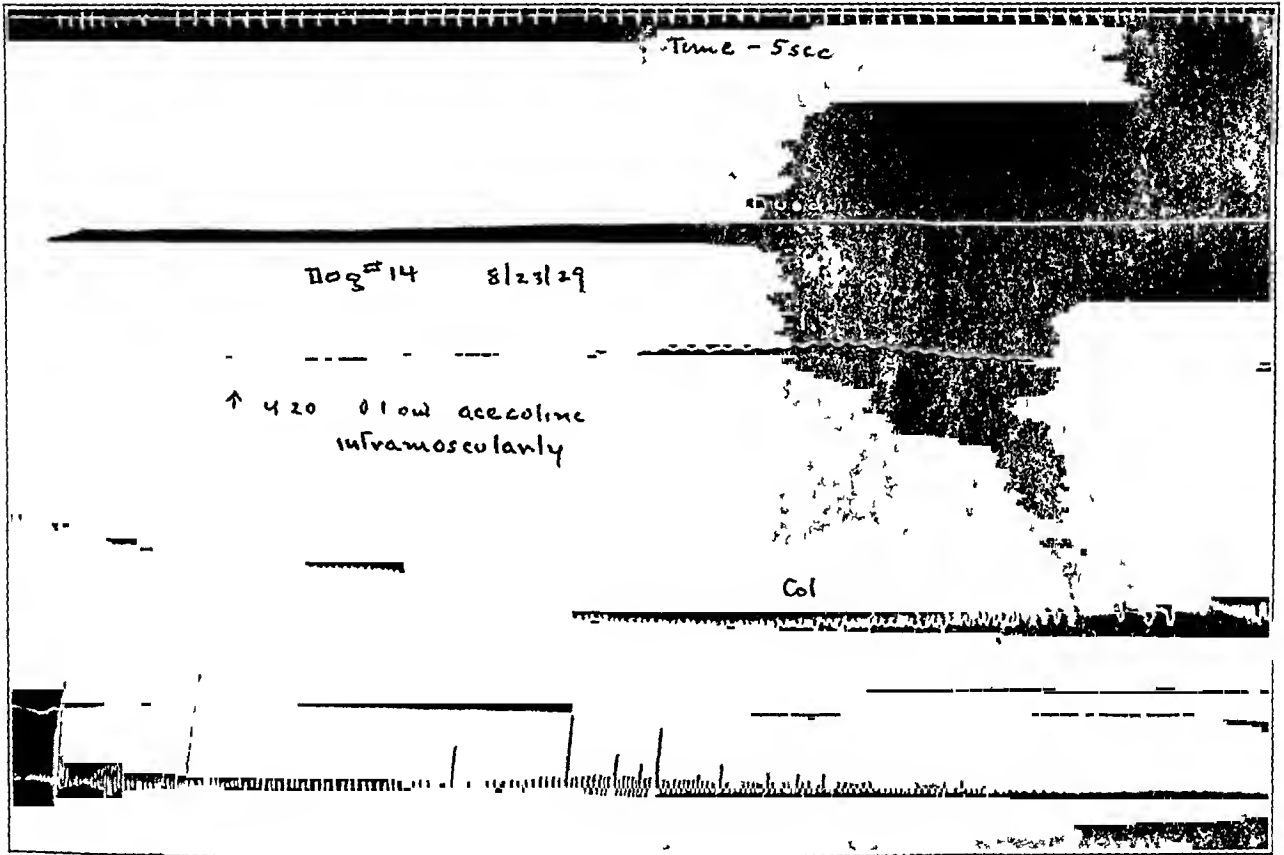


Fig 12—Kymographic tracing showing the effect of the intramuscular injection of 0.1 Gm of acetyl choline into a normal dog. The effect shown on the blood pressure is typical, manifesting a gradual decrease to a low level which is subsequently maintained. Duodenal, ileal and colonic tracings are recorded. Little or no effect is noted on the duodenum. In the ileum, a slight increase in tone and a slight increase in amplitude of movement is recorded. In the colon, no change of either tone or amplitude is seen.

temporarily increased the blood volume. This view seems to be corroborated by the fact that two of the three animals that showed initial depressions of the blood pressure showed subsequent increase, one to a level of 30 mm and the other to a level of 60 mm above normal.

(b) Effect on Intestinal Tone and Motility The effect of this drug on intestinal tone and motility was inconstant and insignificant. In only

one of the four animals was an increase in the tone noted, and this was relatively slight, 8 mm. The effect on the amplitude of intestinal movement was inconstant. One animal showed no effect, another animal showed an insignificant increase (1 mm), and the remaining two animals showed insignificant decreases in the amplitude of movement.

*Effect of Acetyl Choline*—Acetyl choline was injected subcutaneously ten times into as many normal animals.

(a) *Effect on the Blood Pressure* The invariable effect of acetyl choline on the blood pressure was a decrease which occurred either immediately or within a period of five minutes. The decrease averaged 66.6 mm of mercury, which is a considerable depression. In all but

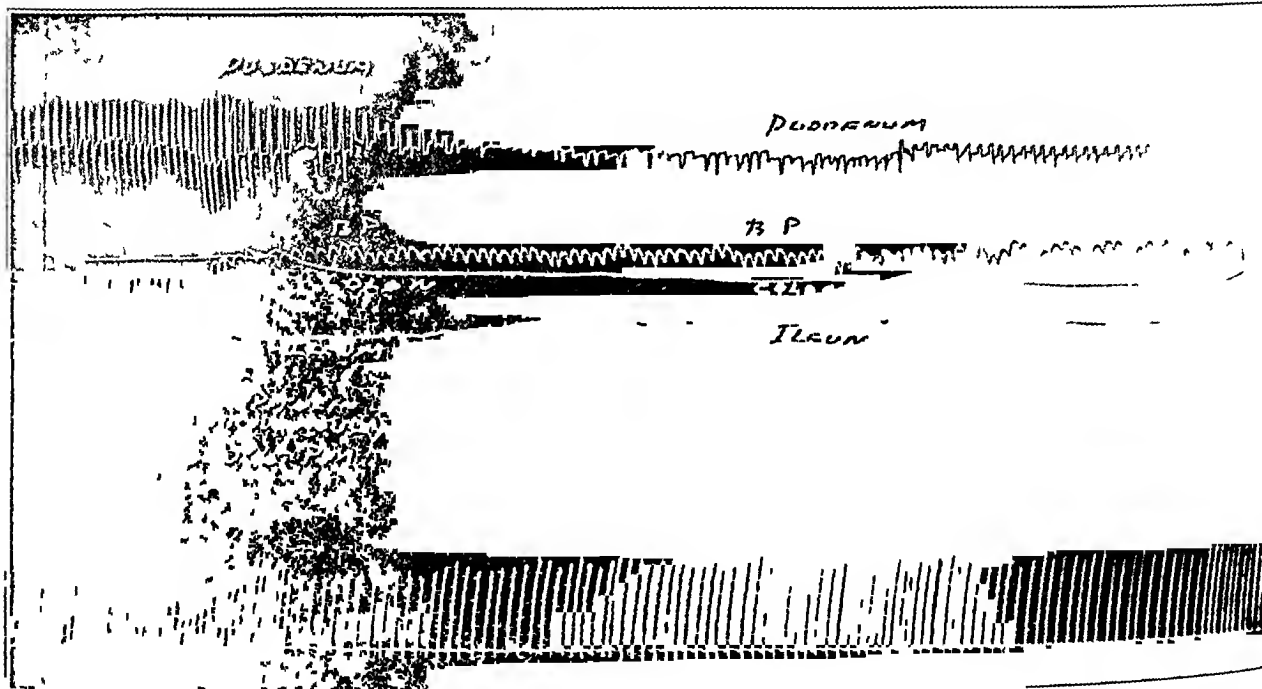


Fig 13—Kymographic tracing, showing the effect of the intravenous injection of 1 cc of pitocin into a normal dog. The blood pressure is relatively unaffected, but possibly slightly increased. The effect on the duodenum in this particular case was a diminution in the amplitude of duodenal movements. In the colon there was relatively little effect, except possibly a slight decrease in tone. In the ileum there was possibly a slight increase in tone and possibly also some increase in intestinal movement.

three of the cases the blood pressure remained subsequently at a relatively constant low level. In two of the remaining cases the blood pressure increased gradually, but never attained a normal level. In only one case did the blood pressure subsequently surpass the normal value.

(b) *Effect on the Intestines* The effect on the intestinal tone was variable. In four cases, 40 per cent there was an increase, averaging 21 mm. In five cases decreases were seen, averaging 6 mm, and in one case no change was noted. The effect on the amplitude was also

variable but was generally in the direction of increases. In six cases the increase of amplitude averaged 4.3 mm. Three cases showed decreases in amplitude averaging 2 mm, and in one case there was no apparent effect on the animal.

*The Effect of Pitocin*—One cubic centimeter of pitocin was injected intravenously into each of five normal animals.

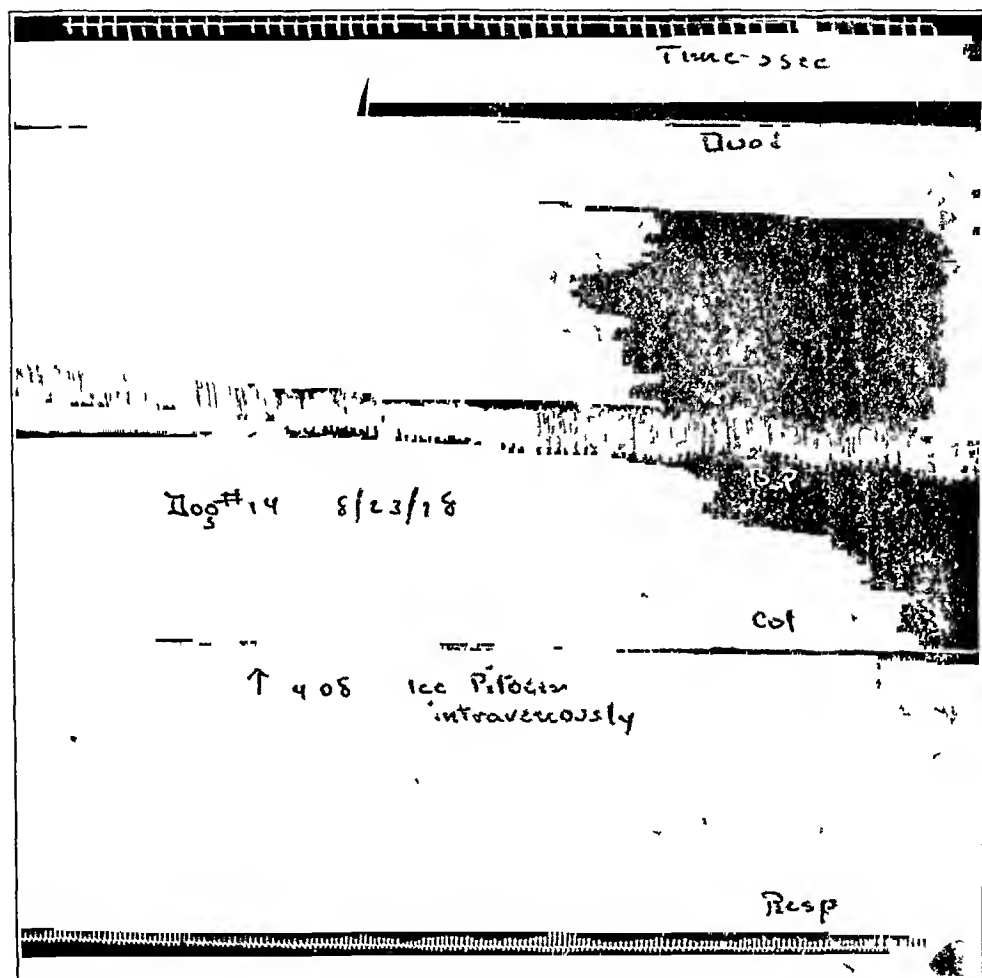


Fig 14—Kymographic tracing, showing the effect of the intravenous injection of 1 cc of pitocin into a normal dog. The only effect seen in this tracing is on the blood pressure, and in this case there was a progressive decrease. No effect on either tone or amplitude of intestinal movement was seen in the duodenum, ileum or colon.

(a) Effect on Blood Pressure. No conclusions can be drawn as to the effect of pitocin on the blood pressure since in two cases no effect was recorded, in two cases increases of 6 and 10 mm of mercury, respectively were found, but one of these cases, the latter showed a subsequent decrease of blood pressure to 50 mm below normal the

latter low level being sustained. In the other animal there was a progressive, slow decrease in blood pressure of 30 mm.

(b) Effect on the Intestines. No constant effect on the intestine was noted when pitocin was used. In all cases in which this particular drug was administered simultaneous tracings of the ileum, duodenum and colon were recorded. As to the effect on tone, in no case was an increase noted in the ileum. In one instance the tone of the duodenum was increased, and in another it was decreased, whereas in two cases the

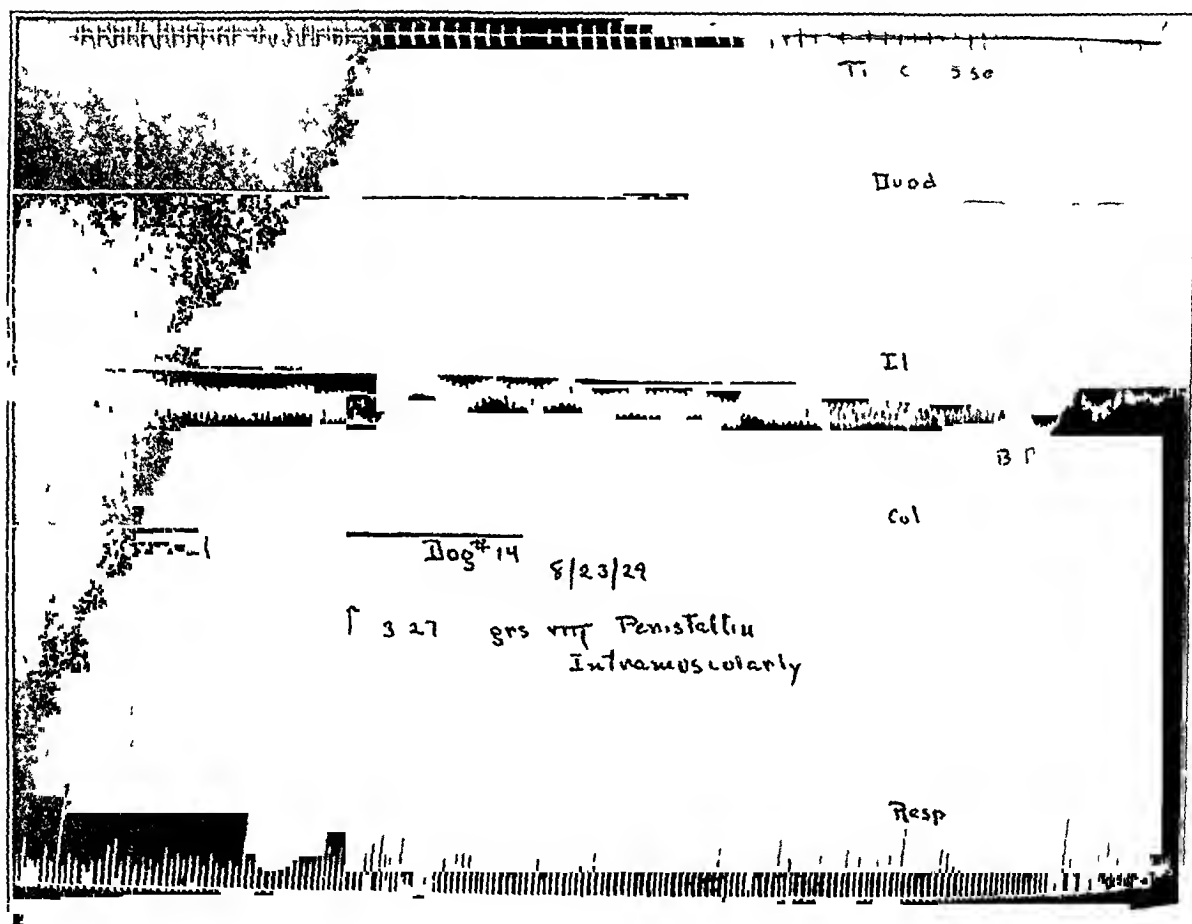


Fig. 15—Kymographic tracing, showing the effect of the intramuscular injection of 8 grains of peristaltin into a normal dog. The tracing is typical in that no significant effect is noted in the blood pressure or in the tone or amplitude of intestinal movement in the duodenum, ileum or colon.

tone of the colon was definitely decreased. The effect of this drug on the amplitude of intestinal movement was variable, sometimes slight increases were noted and at other times slight decreases.

(c) Effect on Respiration. Pitocin showed no appreciable effect on the respiration.

*Effect of Peristaltin*—The effect of peristaltin was recorded fifteen times in twelve animals. It was employed in five instances on four animals with obstruction and ten times in eight normal animals.

The effect of peristaltin on normal animals was as follows

(a) Effect on Blood Pressure Peristaltin showed no constant reaction on the blood pressure of normal animals. There was a decrease in blood pressure in five cases, averaging 12 mm. In two cases there was an increase in blood pressure of 10 mm each. In the remaining cases no change was evident.

(b) Effect on Intestinal Movement The effect of peristaltin on intestinal movement was either nil (four cases) or in the direction of decreases (six cases) with an average of 8.3 mm. The effect on the amplitude of intestinal movement was usually negligible. It was nil in four cases. Decrease in amplitude occurred in five cases, the average being 1.1 mm, and there was an insignificant increase of amplitude in one case (1 mm).

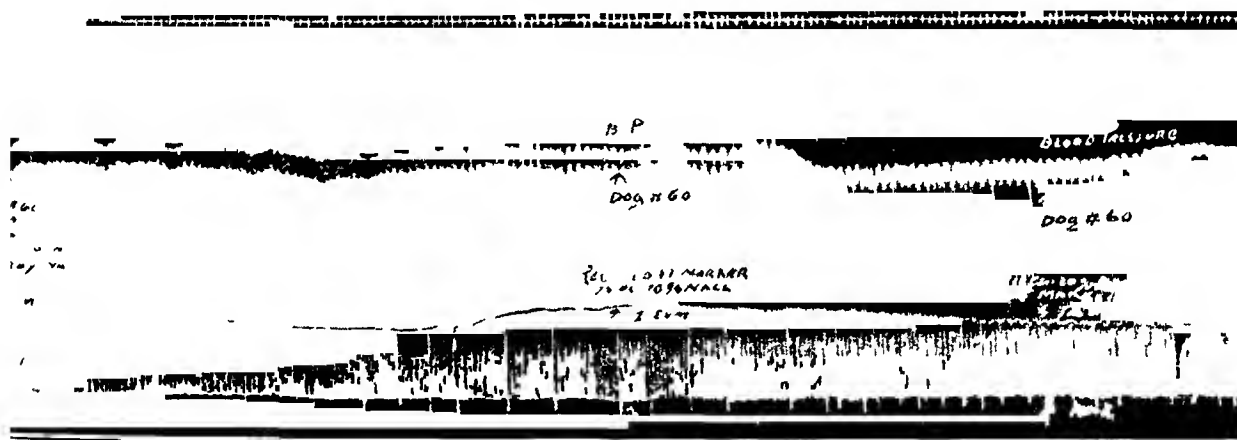


Fig 16—Kymographic tracing, showing the effect of the intravenous injection of 20 per cent sodium chloride solution. No significant effect is noted on the blood pressure. The ileum shows a slight increase in tone, lasting four minutes. At the end of this period, intestinal movement is increased slightly. The respirations show an increase in rate and amplitude.

(c) Effect on Respiration In thirteen of the eighteen cases no respiratory changes were noted, and in the other two cases the effect was questionable.

The effect of peristaltin on animals with obstructed guts was as follows

(a) Effect on Blood Pressure In the five cases in which peristaltin was used three of the animals showed decreases in blood pressure, averaging 20 mm. In two of the animals no change was noted. In the two cases which showed decreases in blood pressure the low blood pressure level was maintained.

(b) Effect on Intestines The effect on the intestine was inconstant with respect to both tone and amplitude of movement. Three cases

showed increases of tone, averaging 102 mm. One case showed no effect on tone, and the remaining animal showed a very distinct decrease to 65 mm below normal. The effect on the amplitude of intestinal movement was of no significance except in one case. In this case, an increase of amplitude of 4 mm was demonstrated.

(c) Effect on Respiration. The effect of peristaltin on the respiration was negligible.

*The Effect of Sodium Chloride*—Sodium chloride in 20 per cent solution was injected intravenously into four animals, two of these were normal dogs and in two of them the gut had been obstructed for forty-eight hours.

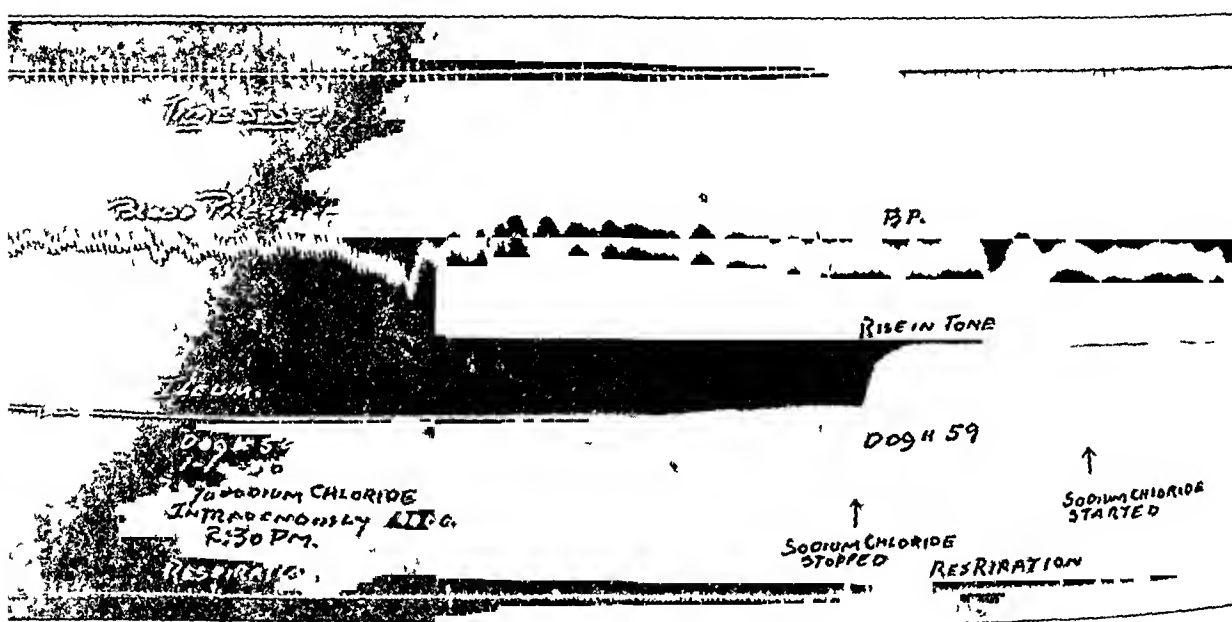


Fig 17—Kymographic tracing, showing the effect of the intravenous administration of 20 per cent sodium chloride solution. The blood pressure is irregular and shows a slight tendency toward progressive decrease. After a later period of about eight minutes, the ileum undergoes a rapid increase in tone, which is fairly well sustained subsequently. Very slight intestinal movement is initiated. The effect on respiration is an increase in rate without apparent increase in amplitude.

The effect of sodium chloride on normal animals was as follows:

(a) Effect on the Blood Pressure. The effect on the blood pressure was variable. In one animal slight variations in blood pressure were noted but no significant increase or decrease eventuated. In the second animal the blood pressure decreased 20 mm within a period of two minutes. This depression of blood pressure was sustained.

(b) Effect on the Intestine. In the first animal a progressive increase in tone of 14 mm was noted, which attained its maximum at

the end of five minutes. In the second animal no increase in tone was noted. The effect on intestinal movement was slight, but both animals showed very feeble intestinal movement at the end of a ten minute period.

The effect of sodium chloride on animals with obstruction was as follows:

(a) *Effect on the Blood Pressure* The effect on the blood pressure was variable. In one animal the blood pressure increased with variations over a period of eleven minutes and attained an elevation of 20 mm of mercury. In the other animal a decrease in blood pressure of 40 mm occurred within one-half minute. The blood pressure did not remain depressed to this low level, however, but subsequently increased 20 mm during the course of the next three minutes.

(b) *Effect on the Intestines* In both animals a gradual, progressive increase in tone was observed. This amounted to 48 mm in the first animal, and reached a maximum within a period of thirteen minutes. In the second animal the maximal increase was 6 mm, attained at the end of five minutes. In both animals increases in motility were noted. The increase in amplitude of intestinal movement of the first animal amounted to 5 mm and in the second animal to 2 mm.

#### COMMENT AND CONCLUSIONS

In view of the relatively large number of clinical and experimental observations that have been made on the effect of drugs on intestinal motility, it would have seemed reasonable to suppose that much more significant changes could be achieved by drug therapy than we have been able to observe. Of more than passing significance would seem to be the inefficiency of pituitary extract as an intestinal stimulant.

Careful examination of the literature with respect to the action of pituitary extract discloses two interesting facts: (1) Most of the favorable reports that have been made on this action of pituitary extract have had their basis in clinical observations, and (2) such experimental investigations as have been made under carefully controlled conditions show a relatively equally divided difference of opinion, virtually as many authorities expressed the conviction that pituitary extract depresses the tone and motility as expressed the opposite and more generally accepted view. Clinicians labor under a severe handicap in the evaluation of the action of drugs, since the psychic reactions of the clinical observer are apt to warp his judgment. There is a real tendency for clinical exaggeration of the beneficent clinical effects and a tendency to underestimate the number and degree of clinical failures.

Our results would appear to be in line with those obtained by the more careful and unprejudiced experimental investigators who have



previously published reports on the action of pituitary extract. Pituitary extract would not only seem to be an ineffective drug in the treatment for intestinal atony, but also would appear to be a dangerous drug in such a condition. Although it sometimes seems to increase the tone and motility of the intestinal musculature, the more characteristic effect is one of decrease in tone and motility. The occasional beneficial effect that might result from injection of the drug in certain cases would seem to be far outweighed by the depressant effect, which is apparently more frequently seen and is comparatively more profound. The variable effect of pituitary extract on the blood pressure is probably not sufficiently appreciated, although in most cases dependence can be placed on pituitary extract to raise the blood pressure, there are apparently cases in which actual depressions occur.

The effect of physostigmine on the intestinal tone and motility, according to our investigations, is virtually that which might be expected from a consideration of previous reports, both clinical and experimental. Although it is true that physostigmine seems never to produce significant decreases in tone and motility and therefore could scarcely be considered a dangerous drug, the stimulating effect of physostigmine would not seem to be particularly significant. The fact that this drug is perhaps the oldest substance that has been used for the purpose of stimulating intestinal motility suggests that physostigmine perhaps has some definite place in the therapeutics of intestinal atony. This is the only drug that we have found to be of consistent efficacy, and possibly the fact should be stressed that the action of this drug seems to be enhanced in intestinal obstruction, at least in intestinal obstruction no further advanced than that used for the purposes of the present experimental investigation. This presents rather interesting evidence that possibly the obstructed intestine, in the initial stages at least, is hyperexcitable, if this is correct, the value of the various other drugs used in this series of experiments would seem to be proportionately minimized. If these drugs are of no value in the stimulation of intestinal movement in a hyperexcitable intestine, they should certainly prove of no value in stimulation of the normal intestine or in an intestine in which for one reason or another the excitability is decreased.

Choline, acetyl choline, pitocin and peristaltin have proved disappointing in the present series of investigations. Apparently little dependence can be placed on these therapeutic agencies in the stimulation of either normal or hyperexcitable intestinal musculature. All in all, it would seem that the drug therapy for intestinal atony rests on a rather precarious foundation, and although the results of the present experimental investigations are by no means conclusive, they suggest a well nigh complete revision of our evaluation of the efficacy of drug therapy in the relief of conditions of intestinal quiescence.

# COMPLETE OCCLUSION OF THE SUPERIOR VENA CAVA BY PRIMARY CARCINOMA OF THE LUNG\*

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Partial obstruction of the superior vena cava is not uncommon. On the other hand, complete obliteration either by compression or by thrombosis is unusual, and obliteration due to carcinoma is extremely rare.<sup>1</sup> I shall therefore in this communication note the instances reported in the literature, describe this condition and add thereto a case observed in Mount Zion Hospital.

## CASES RECORDED IN THE LITERATURE

The first case of obstruction of the superior vena cava was noted in 1806, by Corvisart. At intervals since then cases have been reported and collected as follows: Oulmont,<sup>2</sup> 1856, Fischer,<sup>3</sup> 1904, Rauth,<sup>4</sup> 1911, and Dana,<sup>5</sup> 1922. Dana, after a critical review of all previously tabulated cases, accepted reports of interference with the circulation in the superior vena cava by "primary carcinoma" of the lung in twenty-three instances, only six of which were verified as carcinoma, and by carcinoma primary in the bronchi in fourteen observations. To these must be added Dana's own proved case, bringing the total to thirty-eight. My search of the literature fails to reveal any further reported cases.

Approximately one half of the cases of complete obstruction of the superior vena cava by primary carcinoma of the lung or bronchus showed invasion of the walls of the cava. In the remaining half, the obstruction was due to compression by the tumor mass with or without thrombosis of the cava. The case to be reported in this paper is one of primary peribronchial carcinoma, with complete obstruction of the superior vena cava by compression plus thrombosis.

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\* Submitted for publication, March 25, 1930.

<sup>1</sup> From the Thoracic Surgery Clinics of Mount Zion Hospital and the University of California Medical School.

1 Osler, William. On Obliteration of the Superior Vena Cava, *Bull Johns Hopkins Hosp* **14** 169 (July) 1903.

2 Oulmont. *Soc med d'observation* **3** 463, 1856.

3 Fischer. *Inaug Diss*, Halle, 1904.

4 Rauth. *Inaug Diss Univ zu Giesßen Borna-Leipzig* Robert Noske, 1911.

5 Dana, H W and McIntosh, R. Obstruction of the Superior Vena Cava by Primary Carcinoma of the Lung. *Am J M Sc* **163** 411 (March) 1922.

## ETIOLOGY

Occlusion of the superior vena cava by either compression or thrombosis may be brought about by any one of several factors. Aneurysm of the aorta and mediastinal tumors have been found to be responsible for the condition in about 55 per cent of the 300 odd cases reported in the literature, each in approximately the same frequency. Carcinoma of the lung, bronchi and adjacent organs produced the obstruction in about 25 per cent more of the instances. The remaining 20 per cent are ascribed to various diverse factors relatively infrequently observed. In this group have been noted such causes as mediastinitis, periaortitis, contraction of scar tissue, especially tuberculous or syphilitic, compression by mediastinal tumors other than carcinoma, ecchymococcus cysts, struma, transportation of carcinomatous masses from distant organs, sclerosis of the bronchial glands, phlebitis and thrombophlebitis.

Whereas aneurysm is doubtless becoming more infrequent because of modern antisiphilitic therapy, carcinoma appears to be on the increase. Likewise, inflammatory lesions as a factor in producing the obstruction of the cava appear with greater regularity in the more recent reports. Inflammatory lesions extending into the mediastinum cause traction and pressure on the adjacent organs (i. e., vena cava superior) through induration of the connective tissue. This formation of firm, indurated new growth of connective tissue in the mediastinum has been termed indurative (or adhesive) mediastinopericarditis. Clinically, this condition is characterized by pulsus paradoxus and turgescence of the jugular veins. The commonest cause is inflammation of the bronchial glands, which may be due to syphilis or tuberculosis. Severe rheumatic pericarditis sometimes produces an inflammatory reaction that may extend to the surrounding fibrous tissue, such as the pleura, and along the large vessels.<sup>6</sup>

Thus, when one is confronted with a patient whose symptoms suggest compression or occlusion of the superior vena cava, intrathoracic cancer should first be considered, then "adhesive mediastinopericarditis" and its causes and finally the other varied etiologic factors that have been enumerated.

## SIGNS, SYMPTOMS AND PROGNOSIS

The physical signs and symptoms of occlusion of the superior vena cava are variably striking, depending on the rapidity with which the occlusion takes place and the degree to which compensatory circulation has been established. Obliteration thereof may exist for many years with good health and a completely effected collateral circulation. Objectively, one may note cyanosis or lividity of the face, suffusion of

<sup>6</sup> Pawel, I. Ein Fall von Verschluss der Vena Cava Superior, *Inaug. Diss.*, Leipzig, 1910.

the conjunctivae, prominence and staring of the eyes, edematous swelling of the neck, arms and thorax, with more or less marked dilatation of the superficial veins of the thorax and upper part of the abdomen, edema and cyanosis of the mucous membranes of the tongue, mouth, pharynx and larynx<sup>7</sup> Subjectively, this venous engorgement may produce headache, vertigo, deafness, epistaxis, tinnitus, visual disturbance and somnolence or temporary loss of consciousness<sup>8</sup>

The prognosis depends primarily on two factors (1) the rapidity of development of the occlusion, or the time allowed for the development of a compensatory circulation, and (2) the prognosis in the disease entity that is the primary cause of the obstruction or thrombosis of the cava

#### REPORT OF A CASE

*History*—I A, a man, aged 65, was referred by Dr L I Grodsky, on May 1, 1929, with a chief complaint of swelling of the face and neck Until one month before admission, the patient had considered himself to be in good health Since then he had noted a fluctuating swelling of the face and neck, worse on getting up in the morning, somewhat decreased by night, but on the whole gradually increasing in severity There was no difficulty in respiration or deglutition There was no cough or sputum or history of recent infection of the mouth or respiratory system There had not been noted any loss either of weight or strength His occupation was carpet laying, but he had been unable to secure work for the past two months

The patient was born in San Francisco and had lived there his entire life His general health had always been good He said that he had rarely had any illnesses, except a mild cold, one per year He had not had diphtheria, influenza, whooping cough, asthma, bronchitis, pneumonia or tonsillitis

About two years before, he had had an appendectomy for acute appendicitis and a hemorrhoidectomy He had had no headaches and no trauma His vision had been good, and the eyes were free from inflammation and pain He had had no loss of hearing, and no pain in the ears or discharge He had had no colds in the head, discharge, epistaxis or symptoms of obstruction He had not consulted a dentist for ten years He said that he had not had tonsillitis, sore throat, sore mouth or hoarseness, and no pain in the chest, cough, sputum, dyspnea, orthopnea, palpitation, night sweats or hemoptysis His appetite had been good The bowels had been regulated with an occasional cathartic, but there had been no gastric distress, nausea or vomiting He had never been jaundiced He had never had bloody, tarry or clay-colored stools His hemorrhoids, external, had been relieved by operation two years before There had been no dysuria, hematuria, frequency or incontinence There had been nocturia from one to two times a night for the past six years He said that he had not had venereal disease or any symptoms of it He had not experienced vertigo fainting, paralysis or muscle pains His weight had been constant at about 165 pounds (74.8 Kg) for the past ten years

<sup>7</sup> Lamb, A R Nelson's Loose-Leaf Living Medicine, New York Thomas Nelson & Sons, 1927, vol 4, p 585

<sup>8</sup> Lihenthal Thoracic Surgery, Philadelphia W B Saunders Company, 1925, vol 1 p 260, footnote 6

With the exception that one sister had died of cancer of the breast, the family history was essentially negative.

*Physical Examination*—The patient was well developed, well nourished and slightly obese about 65 years of age, sat up in bed, was not in acute distress, cooperated fairly well, was mentally clear and moved about with no apparent difficulty. The voice was rather hoarse, but was said not to have changed for several years.

The skull was symmetrical, with no exostosis, irregularities or tenderness. The scalp was clean, with no scars. The hair was normal in texture and distribution. There was generalized alopecia of the scalp. The face was round, flushed and edematous especially at the angles of the jaw and in both parotid regions. The skin of the face and tissues above the clavicles and the sternum showed flushing, gradually fading over the shoulders. It was normal in texture, moisture and



Fig 1—Discoloration of the face and neck due to venous congestion, prominence of the external jugular veins especially on the left and swelling of the face and neck.

pigmentation. The eyes revealed beginning arcus senilis. They reacted to light and distance. The vision was good. The fundi showed moderate bilateral choked disks and marked distention of the retinal veins. There was right internal strabismus. The hearing was good. There was no discharge or tinnitus. The nose showed no deformity, obstruction or discharge. The lips revealed moderate cyanosis, and no ulcerations or fissures. The gums showed slight pyorrhea and no lead line. The tongue protruded in the midline, without tremor. The tonsils were small, without exudate or inflammation. The floor of the mouth and the upper part of the pharynx appeared edematous, but not inflamed. The results of laryngoscopic examination were negative.

The entire neck was enlarged, apparently by an edematous infiltration, to at least twice its normal size. The thyroid gland was not palpably enlarged. The veins of the neck were markedly distended on both sides. There was no bruit, stiffness, thrill or abnormal pulsations and no tracheal tug. The lymph nodes

were not enlarged. Over the left clavicle was a small wound where two days before an unsuccessful attempt had been made to remove a node for microscopic examination.

The thorax was symmetrical and moderately barrel-shaped, the expansion was fair and equal on both sides. The respirations were 24 and regular. There was no abnormal pulsation. The venules of the lower half of the anterior wall of the chest were markedly prominent. The breasts were normal.

The action of the heart was regular, the sounds clear, with no murmurs. The right border was 2 cm. from the sternum, the left, 9 cm., the apical impulse was seen and felt in the nipple line, fifth space, 8 cm. to the left of the midsternal line. The rate was 90 per minute.

The aorta revealed no palpable or audible abnormality. Extending downward 7 cm. from the clavicle on the right and 3 cm. to the right of the sternum was an area of increased dullness. A corresponding area of dullness, most marked on the right, was made out posteriorly between the scapulae. The arteries showed radial pulses equal and synchronous, 90 per minute and of good quality. The radial and brachial arteries were moderately sclerosed. The jugular, axillary and brachial veins were markedly enlarged, tortuous and engorged. The blood pressure in the right arm was 115 systolic and 70 diastolic, that in the left arm was 120 systolic and 75 diastolic.

The lungs showed paravertebral and parasternal dullness, as noted. A few scattered moist râles were heard throughout the chest. Tactile fremitus was normal.

The abdomen was soft, lax and tympanitic throughout. No spasm, mass or tenderness was present. There was no free fluid. An egg-sized indirect inguinal hernia on the left was readily reducible. The gallbladder, spleen and kidneys were not felt. The liver showed percussion dullness from the fourth rib. The edge was smooth, and on deep inspiration was felt 1 cm. below the costal margin.

Several pea-sized to walnut-sized masses were felt in both axillae, the largest on the left, apparently these were enlarged lymph nodes. Other lymph nodes were not remarkable.

There was moderate fixation of the dorsolumbar spine.

The extremities showed no involuntary movements, tremor or wasting. There was marked clubbing of all the fingers. No changes in the joints were made out. No varicosities, scars or ulcers were present on the legs. There was no edema of the ankles. The knee jerks were active and equal.

*Laboratory Examination*—The urine, on April 16, 1929, was amber, clear, with a specific gravity of 1.022, and alkaline. It showed no albumin and no sugar or diacetic acid. A sediment contained amorphous phosphates. The Wassermann reaction of the blood was negative on March 17, 1929. Red blood cells numbered 4,470,000, the hemoglobin content was 60 per cent. The white blood cells numbered 5,250, of which 72 per cent were polymorphonuclears, 24 per cent lymphocytes and 4 per cent transitionals. On April 4, 1929, roentgenologic examination of the chest revealed enlarged hilar glands, particularly at the right hilus and infiltration of the right upper lobe (Dr. L. Bryan).

The working diagnosis at this time was that there existed a tumor of the chest with axillary metastases.

*Pathologic Examination*—On May 2, the left axilla was opened in the hope of removing a large lymph node for pathologic examination. My associates and I were surprised to find, on dissection, that the numerous masses in the axilla were not nodes but varices of the axillary vein. However, a small node was removed and the following pathologic report was obtained:

Examination of the lymph node showed only chronic lymphadenitis. The germinal areas were normal. The sinuses were dilated, the blood channels were engorged, the reticular tissue was thickened, and there was some transudation of blood into the pulp. There was no evidence of malignant growth, Hodgkins' disease or lymphosarcoma or tuberculosis.

*Diagnosis*—The diagnosis was chronic lymphadenitis.

*Therapy*—Bronchoscopic examination was considered at this time, but deemed inadvisable because of the marked edematous infiltration of all the structures of the neck. So it was decided to subject the patient to deep roentgen therapy in the hope that in spite of the observations to the contrary, the new growth might be of lymphatic origin and therefore respond to such therapy. Hence the patient left the hospital and reported back at intervals for therapy.

*Second Admission*—On April 15, 1929, the patient returned to the hospital for further study. There had been no change symptomatically or objectively. The results of physical examination were as before, and the roentgen therapy had produced no noteworthy alteration in the suspected new growth. Obstruction to the superior vena cava was now suspected.

Roentgen examination of the chest was repeated, bronchography with iodized poppy seed oil 40 per cent was done, studies of the esophagus with a thick barium sulphate meal were undertaken and an electrocardiographic examination was made. The results of these examinations were reported as follows.

*Roentgen Examination*—On April 22, roentgenograms of the chest, antero-posterior and lateral views, with iodized oil demonstrated normal bronchi at the right base. There was an infiltrating lesion extending out from the right hilus. Probable malignant growth was shown (Dr L. Bryan). On April 27, a roentgenogram of the chest after a thick barium sulphate meal showed no abnormality of the esophagus and no evidence of aneurysm (Dr Levitin). On April 29, roentgenograms of the dorsal spine, anteroposterior and lateral views, showed marked hypertrophic changes about the middle and lower thoracic vertebrae due to hypertrophic arthritis (Dr L. Bryan). On May 2, roentgenograms of the skull, lateral, anteroposterior and postero-anterior views, were negative (Dr L. Bryan).

*Electrocardiographic Examination*—On May 3, electrocardiographic examination by Dr J. J. Sampson showed that there was little shift of the electrical axis, suggesting that there might be adhesive pericarditis.

*Third Admission*—Again, on May 24, the patient was readmitted, complaining of severe attacks of dyspnea and an increasing nonproductive cough. He had fainted twice while out of the hospital.

*Physical Examination*—The essential physical observations at this time were as follows. The pupils were equal and regular and reacted normally to light and in accommodation. The fundi showed marked distention, the nerve head was edematous. The trachea was in the midline. There were no palpable glands. The neck was markedly swollen, and the jugular veins were distended. There were numerous distended veins and venules over the anterior surface of the chest. Expansion was limited at the right apex. There was slightly increased vocal fremitus at the apex of the right lung anteriorly. Percussion showed diminished resonance over the whole chest, but was from dull to flat at the right apex anteriorly and at both posterior bases. There was distant bronchial breathing at the right apex. Breath sounds were diminished at both bases posteriorly. There were no rales. Ten days later there were signs of fluid at the left base.

*Roentgen Examination*—On May 24 roentgenograms of the chest antero-posterior and lateral views, showed no change since the previous examination (Dr Levitt) On June 4, a roentgenogram of the chest showed grayness at the left base due to a small pleural effusion The infiltration of the right upper lobe showed no change (Dr Levitt)



out anteriorly and posteriorly. The left side of the chest was dull anteriorly and resonant posteriorly. The breath sounds were vesicular, but on the right side they were markedly diminished in both the front and the back. The heart sounds could not be heard because of the noisy respiration due to laryngeal noise.

The abdomen was normal. The liver and the spleen were not felt. There was an indirect incomplete inguinal hernia on the left side.

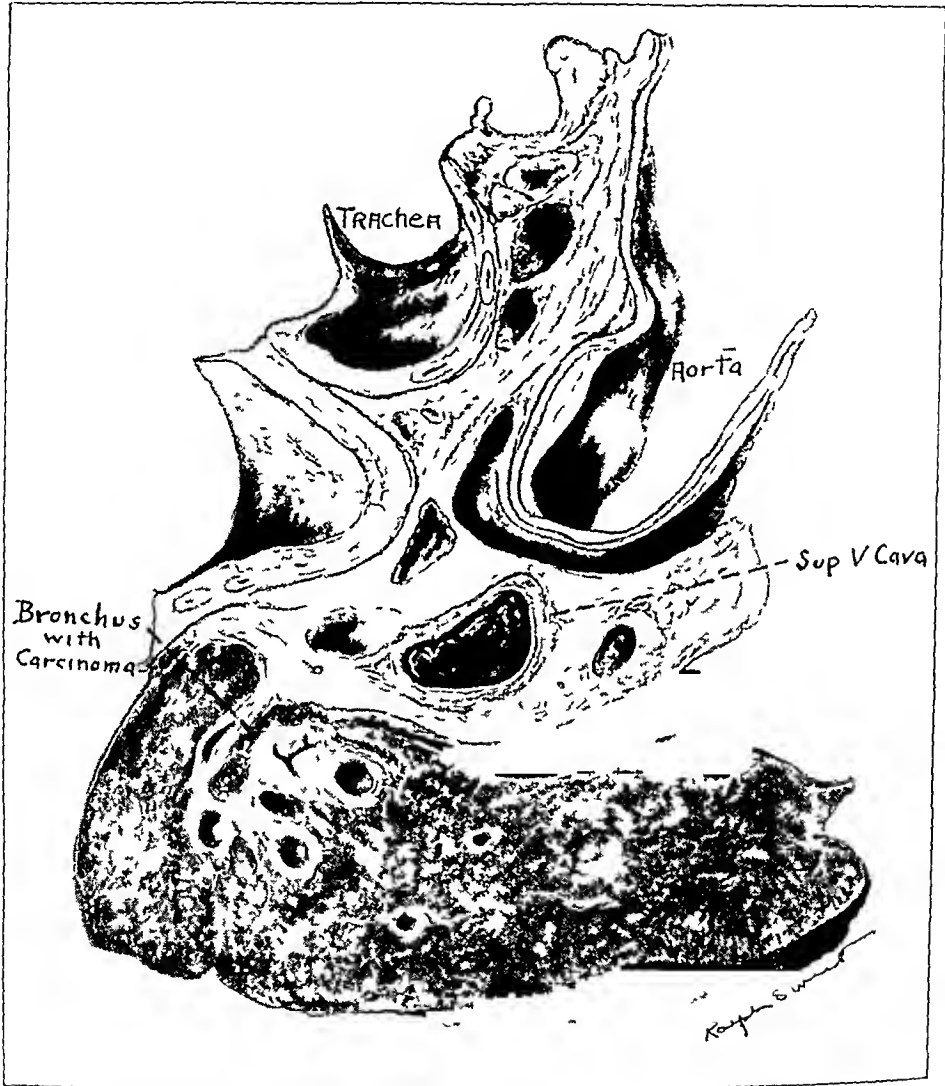


Fig 3—Cross-section of the right upper lobe at the level shown in figure 2, showing peribronchial involvement and thrombus in the superior vena cava.

The extremities were wasted. There was an ecchymotic swelling on the dorsum of the right hand and on the right elbow. The reflexes were normal.

The pulse rate was 92, the respirations were 26 and the temperature was 36.8 C (98.2 F).

The patient was given one-sixth gram of morphine and one-one hundred and fiftieth gram of atropine, and shortly thereafter he went to sleep. One hour later, the pulse rate was 116 and the respirations 32. Fifteen minutes later, the patient had quietly expired.

*Anatomic Diagnosis*—The anatomic diagnosis was as follows carcinoma with peribronchial distribution at the root of the right upper lobe, extension into the adjacent mediastinal tissues, with marked stenosis of the descending vena cava and metastasis to the right suprarenal gland, purulent bronchitis of the right lung, slight pleural transudate in both cavities of the chest, acute splenic tumor, parenchymatous degeneration of the viscera, and thrombosis of the superior vena cava

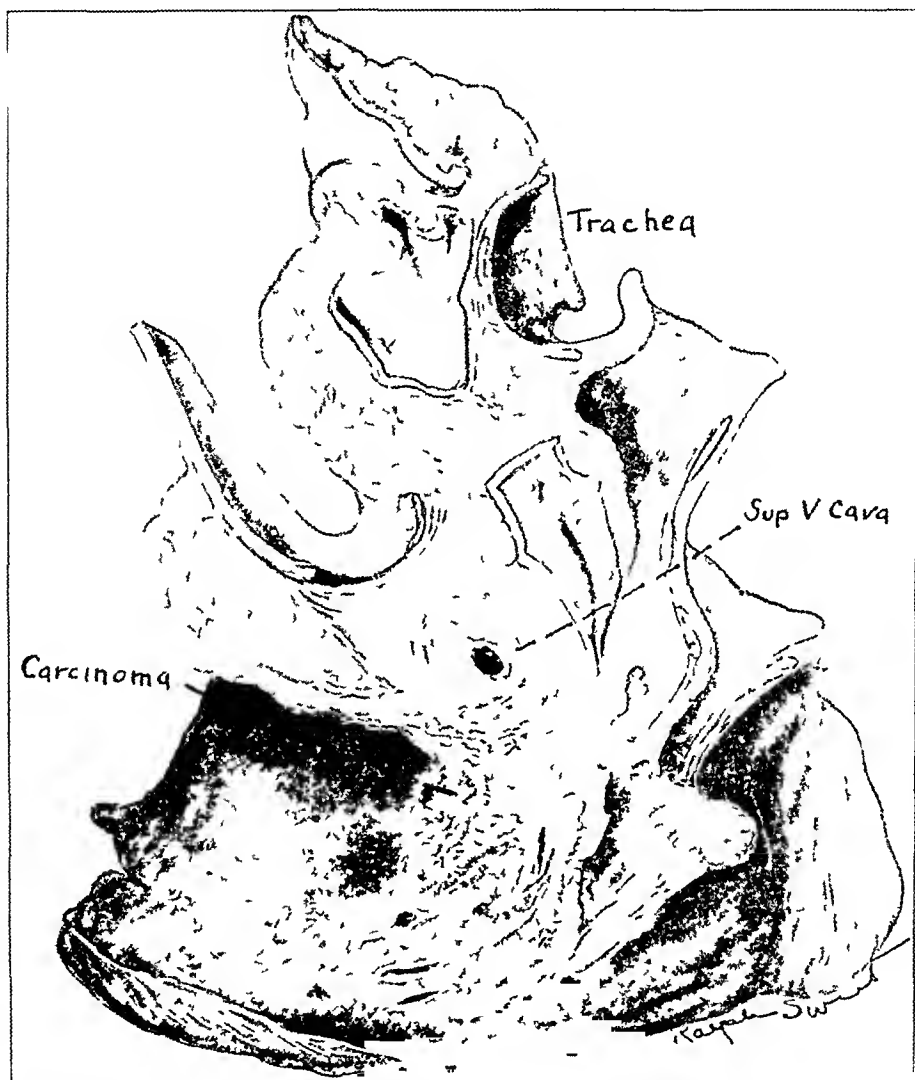


Fig 4—Cross-section of the right upper lobe at the level shown in figure 2 showing the constriction of the superior vena cava and malignant infiltration

*Autopsy*—The postmortem observations as reported by Dr G Y Rusk, were as follows

The remains were those of a moderately undernourished man appearing to be about 60 years of age. Rigor mortis was passing off. There was moderate post-mortem lividity. The pupils were circular equal and midwide. The eyes showed internal strabismus. The neck was thick with deep-seated induration but without any palpable nodules. The axillary nodes were moderately enlarged slightly more so on the left. The inguinal nodes were nodular and somewhat increased in size, more so on the right. The abdomen showed an old, well healed

site of incision for appendectomy. There was no edema of the extremities. The left side of the chest showed an extensive mottled hyperemia.

When the usual median incision was made, the subcutaneous tissues over the sternum were edematous, those of the abdominal wall were normal. The right side of the chest contained about 300 cc of transudate. The left lung showed scattered chronic adhesions over the apex and on the posterior and mesial surfaces of the upper lobe. There was about 200 cc of transudate in the left side of the chest. The pericardial cavity was normal. The peritoneal cavity showed chronic perisplenic adhesions and chronic villose adhesions about the region of the appendectomy.



Fig 5—Photomicrograph of the lung and bronchus, showing the tumor lifting up and penetrating the bronchial mucosa (from the left)

The heart was of normal size. The tissues were moderately softened, apparently from postmortem alteration. The endothelium of all the chambers, including the valves, was normal. The first portion of the aorta was normal. The myocardium was somewhat pale, cloudy and softened, no areas of fibrosis were seen. The coronary vessels were essentially without changes.

The left lung showed the usual pigmentation to a moderate degree. The right lung was removed, with the pericardium and the mediastinal contents. On introduction into the superior vena cava, a probe about 2 mm in diameter met with distinct resistance about 1 cm above the pericardial opening. The right lung was of normal size. At the inner aspect of the upper lobe near the hilus, there was an ill defined palpable mass that felt denser in the adjacent mediastinal tissue.

A section of the trachea and bronchi to the upper lobe showed the mucous membranes hyperemic. No ulceration of the mucous membrane was seen, but encircling the bronchus of the upper lobe was a layer of dense white tissue varying in thickness up to about 25 mm, fairly localized on the pulmonary side, but continuous with a nodule, about 25 cm in diameter, that extended into the mediastinum. Through the center of this nodule ran the markedly stenosed superior vena cava. Beyond the growth in the pulmonary tissues there was a thin, mucopurulent exudate. The encircling of the bronchi by the growth, while making the walls rigid, apparently caused no appreciable narrowing of the lumina. Section of the lower lobe showed hypostasis and mucopurulent exudate in some of the larger bronchi.

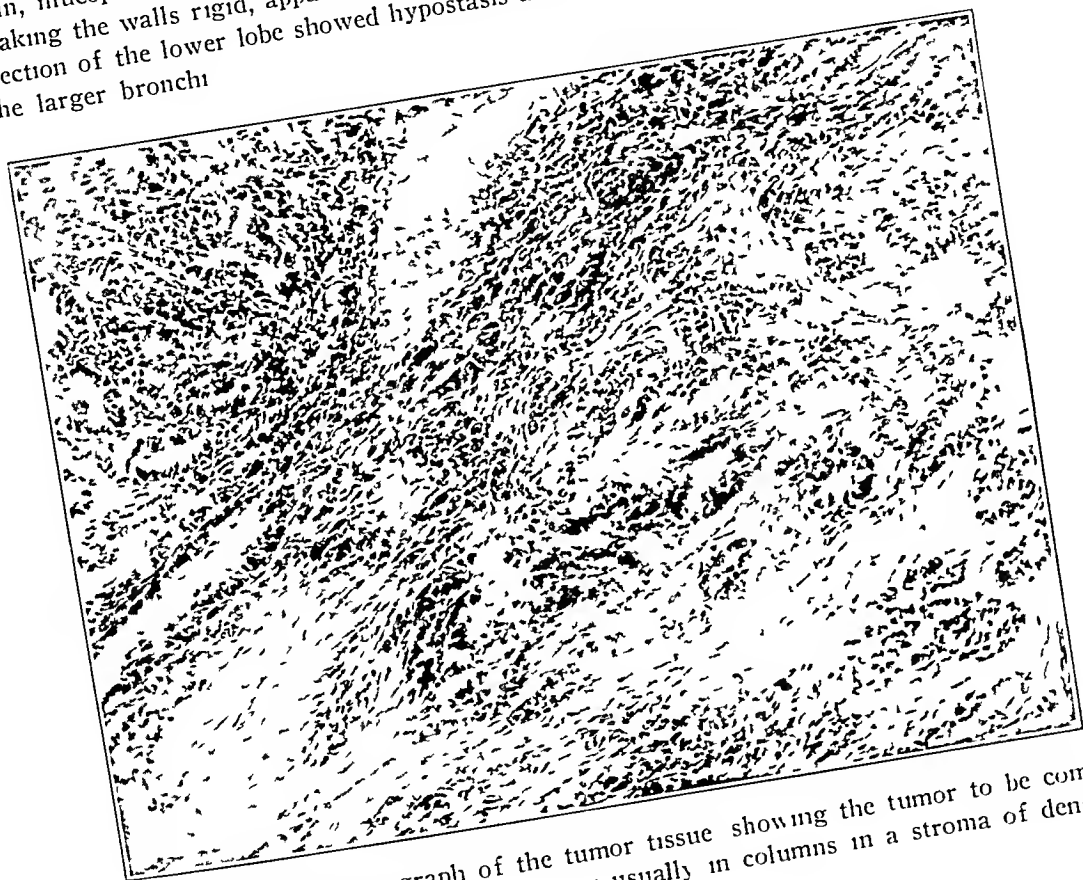


Fig 6—Photomicrograph of the tumor tissue showing the tumor to be composed of large and small cells growing usually in columns in a stroma of dense fibrous tissue.

The spleen was increased to about twice its normal size and was soft. The capsule was torn in several places, the sites of adhesions. On section the tissues were grayish red and soft and the anatomic details were obscure.

The liver was of normal size. On section, it showed slight cloudy swelling but was otherwise normal.

The right suprarenal gland was moderately enlarged. On section it showed a firm, white, irregular mass of tissue that was apparently a metastasis from the carcinoma. The left suprarenal gland was normal.

The kidneys were moderately reduced in size. The capsules stripped with moderate readiness. On section there was some increase in the peripelvic fat. The tissues were somewhat grayish but the architecture appeared fairly well preserved.

The gastro-intestinal tract was normal, the urinary bladder and prostate were normal, and the pancreas appeared to be normal. The retroperitoneal lymph nodes were soft and hyperemic. The abdominal aorta showed a moderate amount of atheroma without ulceration or calcification.

The central nervous system was not examined.

Sections of the superior vena cava showed a definite thrombosis with considerable organization. The process must have been of at least several weeks duration.

*Histologic Examination of the Tumor*—Histologic examination of the tumor by Dr. Zera E. Bolin showed that it was composed of large and small cells usually growing in columns in a stroma of dense fibrous tissue. The cells varied from round to oval, unless compressed, in this case they were spindle-shaped. The nucleus was oval and stained deeply. Many mitoses were seen and a moderate number of atypical mitoses. The protoplasm was eosinophilic. In lymph nodes and other places where there was but little pressure, the cells tended to arrange themselves in small alveoli. There were, as a rule, from four to eight cells in a group. No cilia could be found in these alveoli, nor could any evidence of secretion be found. The fibrous stroma was dense and made up about two thirds of the tumor. A moderate number of mononuclear cells were found in the stroma.

*Histologic Diagnosis*—The histologic diagnosis was scirrhous adenocarcinoma of the lung.

# DISRUPTION OF PELVIS WITH LUXATION OF THE INNOMINATE BONE\*

C W PEABODY, M D

DETROIT

Eight patients have been received in the Henry Ford Hospital with unusually severe injuries to the pelvis, all sustaining a complete disruption of the pelvic bone with separation and displacement of one side from the other. In five instances there was separation and displacement anteriorly at the pubic symphysis, with accompanying separation and displacement of one or both sacro-iliac synchondrosis, constituting a true dislocation or luxation of the innominate bone. In the others, instead of separation at the pubic symphysis, there were vertical fractures close to it, with accompanying rupture of the sacro-iliac joint and upward displacement of what was practically the whole innominate bone, making the injury a comparable one. Several patients had accompanying fractures at other points in the pelvic ring but with little or no displacement at these points, so that the most striking lesion seemed to be the displacement of the innominate bone as a whole. One of these patients died, one was not traced, and the rest made a complete recovery.

As seven of these patients came under my care in the space of six years in an institution which has comparatively few cases of major accidents (on the average not more than a dozen beds being occupied in this period by patients with fractures), I gained the impression that this must be a not uncommon type of pelvic injury. Reference to the literature to determine the usual outcome and prognosis, on the contrary, seemed to warrant a conclusion that this was an infrequent lesion, and that the outlook was usually serious.

In using the title 'Luxation of the Innominate Bone' to designate this type of injury, I have taken what seemed the most suggestive anatomic expression. In the literature, however, this term has been used but few times, the main terms employed being pelvic luxation, separation or displacement. Some of these cases have been recorded as sacro-iliac separation and a few as separation of symphysis pubis, and this confusion in indexing with simple luxations of the front or back alone added much to my labor. The German terminology is fairly uniform (incidentally German references comprise a total in excess of all others combined), the term "Luxationen Beckenhafte" usually obtaining

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\* Submitted for publication, March 17, 1930

^ From the Orthopedic Division, Department of Surgery, The Henry Ford Hospital, Detroit

\* Presented originally at Detroit meeting of Central States Orthopedic Society, November, 1927

Only a few instances of triple separations have been reported, that is, separation of both sacro-iliac bones as well as an anterior rupture

References in the literature go back over one hundred years. During this period probably no more than sixty-five cases have been reported, usually as single instances, a few writers reporting two, one four and one six, but this has been the highest personal observation, with the exception of observations on eighteen summarized by one author, six of these being fresh injuries and nine old injuries with persisting displacement. The rapidly increasing observations of the last two decades have certainly established this injury as fairly frequent and as bearing a favorable prognosis. This is in contrast to the attitude of earlier times, when most of the reports were of fatal cases.

In the diagnosis of this lesion it has not been necessary to use roentgenograms, except for confirmation. Serious injury to the pelvis is almost immediately suggested by the complete helplessness, severe shock, the great pain referred to pelvis on any movement, the tenderness on palpation of the synchondroses, and the gross hypermobility of the pelvis to manipulation, if examination is carried this far. In the cases in this report the diagnosis of severe pelvic injury was always made by a senior intern on first examination, and immobilization of the pelvis by a binder and Bradford frame was secured before anything else was done. The degree of hypermobility was appreciated only at the time of reduction under an anesthetic.

The injury seems uniformly to be accompanied by severe initial shock, but rarely by visceral complications. In few of the cases were the latter important, but in most the symptoms of shock were rather prolonged, delaying any vigorous measures of reduction. Fracture, usually without displacement, at some point in the pelvic ring frequently accompanies the innominate luxation, but has seemed to be a less important factor and of little importance as a complication, displacement at the fracture line being slight. Fracture of the lateral process of the fifth lumbar vertebra is also seen in combination. This last accompanying pelvic injury has been illustrated by me in the past.<sup>1</sup> In all the cases in the present series, accompanying fractures of one or another of these types was present.

Although the mechanism of innominate dislocation has generally been considered to be a crushing injury, the victim being squeezed or rolled, with probably a large majority of reported cases having been caused by an accident of this nature, a considerable number have been produced by a straight fall. The series reported here is divided between these types of violence. Nor does either type seem to have a consistent influence on the character of the luxation, i. e., whether it is a simple proximal or posterior displacement of one half of the pelvis or luxation accompanied by excessive rotation.

<sup>1</sup> Peabody, C. W. Unusual Fractures, *J. Bone & Joint Surg.* 4:459, 1922

With or without complete reduction, ankylosis of the involved synchondroses seems invariably to occur. The union at the sacro-iliac joint is usually bony. This seems to confirm observations of many that any extensive traumatic displacement of a sacro-iliac joint will be followed by ankylosis. Although recovery has been found to follow frequently without reduction, the latter seems necessary for complete freedom from disability. Either a scoliosis or a raised shoe are inevitable without more or less complete reduction of any considerable displacement. In most reported cases reduction has been gradual, being obtained by weight extension of the shortened limb, by countertraction and by circular compression of the pelvis. In others, particularly in German cases, reduction has been obtained by manipulation under an anesthetic, followed by retention with a plaster of paris cast, this has sometimes been resected a little in midline and further reduction secured by turn-buckles placed in either a transverse or an oblique position as indicated. Severe discomfort has usually been reported during gradual reduction.

A method of treatment was successfully used in most of the nonfatal cases in this series which is a little different from the methods reported. As soon as the general condition warranted the use of an anesthetic (from a few days to several weeks), the patient was moved on his frame to the x-ray department and placed on the tilting fluoroscopic table used for gastro-enteric observations, the patient's feet being placed at the head end of the table. The foot on the displaced side was made fast to the head of the table, and with anesthesia induced, the mobility of the pelvic girdle was verified by palpation. With the body steadied by the operator and assistant, the table was then tilted nearly to the vertical position, the weight of the body coming finally entirely on the fastened leg. Under fluoroscopic control, the pelvis was very gently manipulated between the hands until replacement could be seen as well as felt, a previously prepared webbing belt was at once placed around the pelvis and buckled tight, the table was returned to the horizontal position, the traction released and the position again checked by the fluoroscope. Where rotary displacement was present, the limb on the anterior side was held down, while the opposite limb, extended at the knee, was strongly flexed at the hip, levering this side of the pelvis forward. When the patient was returned to his room, the Bradford frame, to the end of which the patient's foot was reattached, was left inclined head down. Plaster of paris was not used. To guard against relaxation in bed, 20 pounds of traction was maintained on the leg of the affected side. The binder was replaced for greater comfort by the overhead pelvic sling after return to the fracture bed. In two cases a recurrence of some of the rotation displacement at the symphysis occurred in the second month. In both instances the patient had to be transferred to another wing, being removed from bed for this purpose and although a tight binder is said to have been applied, no control



roentgenograms were obtained for some time afterward. On account of probable infiltration of the soft tissue at the pubis, operation with wiring was then done, little mobility at the back of the pelvis could be obtained at that time.

In case 1 taken from the earlier hospital files, operation performed early by Dr R D McClure with manipulation of the pelvis wiring of the symphysis and fixation in plaster gave a highly satisfactory result. In this case there was no fracture on the displaced side, direct manipulation of the anterior end of innominate bone would probably be effective in reducing displacement in this type of case when early operation is possible. In another case in this series the patient suffered relatively slight displacement posteriorly although there was complete rupture of the sacro-iliac and marked displacement at the symphysis. There was an accompanying ruptured bladder, for which early operation was done. No definite manipulative measures were carried out yet subsequent roentgenograms showed that both luxations had been spontaneously reduced. This was maintained by treatment on a fracture bed until consolidation was complete.

Of the eight patients seen, six were treated to a conclusion. One case was fatal before any definite treatment for skeletal injury could be carried out, and one patient was removed from the institution shortly after admission. In the six concluded cases all the patients recovered without any residual disability referable to the pelvic injury. In all the upward displacement of one side of the pelvis was corrected and consolidation of the pelvic ring was obtained. In two the relations at the symphysis were not entirely normal, and anatomic reposition at the points of fracture was not obtained.

It may be of interest to note that sciatic pain was not a marked symptom, save in the cases showing an accompanying fracture of the lateral process of the fifth lumbar vertebra.

The roentgenograms here shown do not include the first case in which examination was made on glass plates that are no longer preserved. The same is true for case 2, except that on a recent return of this patient for another condition a roentgen examination was obtained and is here shown. The remaining six cases are illustrated by roentgenograms taken before and after treatment.

#### REVIEW OF THE LITERATURE

The well known textbooks in this country dealing with fractures such as those of Wilson, Cotton Scudder and Stimson give rather scant attention to the injury under discussion. Wilson under the title "Separations of the Symphysis" emphasized that this condition must be accompanied by some degree of sacro-iliac luxation if fracture has not occurred, and in discussing sacro-iliac dislocation stated that in complete

dislocation symphyseal separation must have occurred though not showing. The entity of a complete innominate dislocation is not mentioned.

Cotton dealt with this subject under the title "Fractures" rather than "Dislocations," and following a paragraph on "Separation of Symphysis" there is a diagram illustrating a coincident sacro-iliac luxation. The author stated that this double, or even triple, dislocation may occur but must be rare. He stated that there are cases on record, and that the lesion is not as serious as one would expect. One roentgenogram is reproduced showing a complete upward dislocation of one innominate bone accompanied by fracture of the acetabulum, a note reports complete recovery without disability at the end of one year.

Stimson recognized the occurrence of complete luxation and mentioned in addition the universally quoted cases of Malgaigne, Salleron and Crete, also one by Earle in 1835, not elsewhere referred to. He seems to imply that the condition is rare and says "As a rule prognosis is extremely grave."

Scudder, in a recent edition (1928), failed to mention this injury, either in the extensive chapter on fractures of the pelvis, or in the supplement on dislocations.

Case reports of this injury go back to 1820 with a report by a Belgian surgeon, Cloquet. Malgaigne, in 1855, reported six cases with four deaths. Salleron, in 1871, reported four cases, all fatal. Other case reports up to 1900 were single ones totaling twenty-two. Since the beginning of the twentieth century, the cited cases have been more numerous, but still consist of only single instances or of two cases with the exception of a contribution by Haumann, who reported six new cases not noted previously and mentioned also a personal observation of nine additional patients that he had seen some time after injury but who showed persisting displacements. The total since 1900 is forty-one, making in all sixty-three. The accompanying table illustrates the chronological incidence.

Special additional mention should be made concerning some of the contributions. In 1925, Maissonnet had a detailed and interesting paper in the *Paris médical* in which pelvic injuries suffered by horsemen either from shock in the saddle or by fall to the ground are discussed as to the result to be expected from either, and particularly the urinary complications of pelvic injuries. This was apropos of his own cases of innominate luxation in which there was serious urethral and bladder injury but ultimate recovery with moderate disability despite persisting displacement which he considered rather common. There is an extensive bibliography. In the report of Haumann, it is noted that in nine of his whole series there was some type of fracture in addition to the dislocations six patients having this in the same half of the pelvis and three in the opposite half. This did not appear to have complicated the original or final state. All showed a favorable outcome with recovery.

the shortest duration being one month and the longest seven months. In some of the ancient cases observed by him the luxation had been neither recognized nor corrected, but invariably had consolidated. Scoliosis was usually present in these, but to a marked degree in only three. One of the patients in the new series died on the ninth day and another in the eighth month from urinary complications. Of the total number, eight returned to full earning capacity, three others had 10 per cent disability and the remainder 25 per cent, which was the

### Chronological Table

Date	Name	No. of Cases
1820	Cloquet <i>Nouv. I. de med.</i> , vol 7, p 201	1
1835	Earle <i>Med. Chir. Tr.</i> , vol 19, p 257	1
1849	Thouvenet <i>Bull. Soc. anat. de Paris</i> , vol 24, p 29	1
1850	Parmentier <i>Bull. Soc. anat. de Paris</i> , vol 25, p 35	1
1855	Malgaigne <i>Traite des Luxations</i> , Paris	6
1865	Larry <i>Gaz. d. hop.</i> , p 135	1
1868	Dolbraun <i>Gaz. d. hop.</i> , vol 41, p 135	1
1871	Salleron <i>Arch. gen. de med. Paris</i> , vol 3, p 34	4
	Dubreuil <i>Gaz. d. hop.</i> , vol 44, p 413	1
1875	Dupont <i>Arch. med. belges</i>	1
1872	Pollock <i>Lancet</i> , vol 2, p 409	1
1888	Niehaus <i>Deutsch. Ztschr. f. Chir.</i> , vol 27, p 467	1
1890	Hallowell <i>Northwest Lancet</i> , vol 10, p 135	1
1899	Hopkins <i>Ann. Surg.</i> , vol 29, p 601	1
	Total prior to 1900	— 22
1902	Linser <i>Beitr. z. klin. chir.</i> , vol 35, p 94	1
1903	Riedinger <i>Arch. f. Orthop.</i> , vol 1, p 414	1
1905	Tillmanns <i>Ber. d. deutsch. chir. Gesellsch.</i> , Stuttgart	1
1906	Crete <i>Deutsche Ztschr. f. chir.</i> , vol 83, p 391	1
	Stinelli <i>Cong. d. soc. Ital. d. chir.</i> , Milan, vol 19	1
1908	Grünbach <i>Deutsche Ztschr. f. chir.</i> , vol 94, p 609	1
	Lindenstern <i>Beitr. z. klin. Chir.</i> , vol 58, p 709	1
	Warrack <i>Brit. M. J.</i> , vol 1, p 203	1
1909	Felten <i>Hildebrands Jahrb. der chir.</i> , p 1150	1
	Fischer <i>Zentralbl. f. chir.</i> , 1909, vol 38	1
1911	Finsterer <i>Deutsche Ztschr. f. chir.</i> , vol 110, p 191	1
	Guibé <i>Bull. et mem. Soc. Anat. de Paris</i> , vol 86, p 36	1
1914	Heinemann and Siedungrotzky <i>Arch. f. klin. Chir.</i> , vol 103, p 927	2
1917	Webb and Snell <i>Arch. Rad. &amp; Elec.</i> , vol 2, p 33	1
1918	Simpson <i>Ann. Surg.</i> , vol 67, p 348	1
1919	Hirschberg <i>Deutsche med. Wchnschr.</i> , vol 33, p 904	2
1920	Block <i>Deutsche Ztschr. f. Chir.</i> , vol 160, p 113	1
1921	Berard <i>Lyon chir.</i> , vol 38, p 1	2
	Haumann <i>Beitr. z. klin. Chir.</i> , vol 103, p 278	6 recent 9 old
	Moritangard and Moreau <i>Rev. d'orthop.</i> , vol 8, p 415	1
1923	Hermansdorfer <i>Deutsche Ztschr. f. Chir.</i> , vol 183, p 129	2
1923	Cotton <i>Dislocations and Joint Fractures</i> , Philadelphia, W. B. Saunders Co.	1
1925	Marisornet <i>Paris med.</i> , vol 2, p 161	1
	Total since 1900	— 41
	Writer's series	8
	Grand total	— 49

maximum. Roentgenograms showing typical displacement were included in the six cases in which treatment was given.

Hermansdorfer's report in 1923 contained an excellent clinical report of observations and treatment in two cases, with roentgenograms of one. Complete recovery was reported in both, one patient being treated by a spica-jacket cast with the midsection removed down the front and obliquely placed turnbuckles used to reduce the displacement, and the other by early manipulation followed by traction and countertraction in bed and finally the same cast technic. Reduction was not entirely

complete in either case, although solid fixation occurred. The author discussed the previous literature and methods of treatment used by others in his country. Gradual reduction by traction and compression seemed to be more favored than early manipulation, which was held dangerous. He quoted Block as using skeletal traction.

Simpson reported one case with complete recovery after hospitalization of ten weeks and disability over one year. Early reduction by manipulation was carried out and the symphysis was wired. Reduction was found to be incomplete but was later improved by longitudinal traction and lateral cross-traction through windows in the cast that had been applied at operation. His patient had no fractures accompanying the dislocation. He reviewed previously reported cases in which there had occurred nothing but the innominate luxation, he found twelve such instances with a mortality of 25 per cent. In five of the twelve, however, no roentgen evidence had been obtained to rule out the fractures commonly observed by others.

Block, after reporting the critical case of a boy 9 years of age who had a complicating perforating wound of the abdomen but recovered with incomplete reduction and some disability, discussed the subject in some detail, including five other cases in the literature since Finster's report in 1911, one of which he insists must be discarded.

In 1911, Guibe reported in some detail the observations in a fatal case. He also critically reviewed the previous literature, particularly Tillmanns' previous review of eleven reported cases, and, having analyzed these, discarded many for various reasons and held that there were only eight authenticated cases prior to his own, all fatal. Apparently he was unwilling to accept any criteria of diagnosis save autopsy observations.

Finsterer, in an excellent discussion following his own case report of a boy of 12 who made a complete anatomic as well as functional recovery despite a lapse of two weeks before treatment (traction followed by wiring), searched the literature subsequent to Tillmanns' review in 1905 and found eight additional case reports.

Crete, in 1906, further emphasized the earlier ideas that this injury is rare. Though his own cases were fatal, with severe infection in perineal lacerations, he expressed the belief that without such complication there should be a very low mortality rate.

The older single reports were almost invariably of fatal cases, of Malgaigne's six, four were fatal and of Salleron's four, one was fatal.

In seeking conclusions from the literature in general it may be said that as increasing attention is paid to its possibility complete dislocation of the innominate bone is being observed more often and more frequently in nonfatal cases, that though the roentgen examination does not seem necessary for diagnosis increasing recognition of the condition has followed the wider availability of this method of study, that though

the mechanism seems to be more frequently a crushing injury, the displacement can be produced by a severe fall, which, however, is more frequently immediately fatal and so diminishes the likelihood of clinical observation. Without visceral complications, recovery from this unilateral pelvic dislocation can uniformly be expected with or without treatment. Reduction is likely to decrease disability. Reposition is more complete if the procedure is not too long delayed, and manipulation under an anesthetic, if carefully carried out, does not seem to increase the mortality. A review of the literature would seem to indicate that there should be a more extensive recognition of the condition in the textbooks than now prevails.

#### CONCLUSION

Eight acute cases of traumatic dislocation of the innominate bone, with one fatality, are reported. A safe method of early reduction by manipulation is described and recommended. A fairly comprehensive review has been made of the literature, which while probably not absolutely complete, is adequate enough to emphasize the clinical importance of this injury and to allow some general conclusions to be made.

#### REPORT OF CASES

CASE 1—Peter H., a stonecutter, aged 24, was admitted to the hospital on the evening of Nov. 11, 1917, a few minutes after being crushed between a standing and a moving truck. He was conscious at examination and was in great pain referred to the pelvis; this pain became intolerable if the body or limbs were handled. There was marked rigidity of the abdominal and lumbar muscles. He was in a state of considerable shock, with thready pulse, clammy skin, and a blood pressure of 90 systolic and 56 diastolic. The greatest tenderness was noted in the region of the left sacro-iliac joint, of the symphysis and of the perineum, where separation and displacement could be readily appreciated by palpation. Rectal examination did not suggest urethral injury. There seemed to be shortening of the left leg. There was also long, deep laceration down the adductor aspect of the thigh.

Simple cleansing was administered to the wound with sterile dressings, and after the patient was strapped to a Bradford frame, treatment was restricted to combating the shock, which persisted for about three hours. Bloody urine was obtained by catheter the first night, and on tentative diagnosis of a ruptured bladder a retention catheter was inserted. The next day only occasional blood cells were present in the urine. The catheter was withdrawn, and voiding became spontaneous.

Roentgen examination of the pelvis was made on the day after admission. Glass plates were being used at that time and none of these has been preserved. Accordingly, the roentgenographic interpretation is quoted in detail. "The left side of the pelvis does not seem to be in the same plane as the right side. There is no line of fracture seen on this side of pelvis. There is apparently an unusually wide separation of the left sacro-iliac joint. There is marked separation of the symphysis pubis about 5 cm., with riding upward of the right side. There is a double fracture of the right descending ramus of the pubis at the obturator foramen with slight displacement. Diagnosis: Fracture ischiopubic right, dislocation sacro-iliac left, dislocation symphysis pubis."

The patient's general condition improved excellently and though the laceration was slightly infected, it was controlled by Carrel-Dakin technic, a large scrotal hematoma required nothing more than support, and no other complications developed.

On the eighth day, the temperature being normal and the general condition good, persisting dislocation of the symphysis was reduced by open operation with fixation by Lane plates, the pelvis and lower extremities were included in a plaster cast. Convalescence from the operation was entirely uneventful. On the twentieth day, skin was grafted over the granulating wound on the thigh. On the fortieth day, the patient began to sit up in bed, and on the forty-fourth day he was discharged to his home by ambulance.

The patient failed to return for further convalescent treatment or observation, but about three years later responded to a recall letter, reporting in person, in apparent good health and with no obvious disability, stating that he was back at his regular work as a stonecutter. The only subjective symptoms were occasional burning and some pubic discomfort on lifting. Arrangements were made for roentgen examination and physical check up but he failed to return for this and was not seen again. However, testimony as to the resumption of his former occupation would seem to make the result most gratifying in this case. This patient was under the care of Dr. R. D. McClure, who also performed the operation.

CASE 2—Charles D., a Jew, aged 57, short and weighing about 190 pounds (86.2 Kg.), hypertensive in type, came under my care on Nov. 5, 1921, having been admitted to the hospital the previous day following an automobile accident. Details of the accident and of the condition on admission were not available. At examination he was found to be in a rather shaky condition, apparently in great pain and a marked state of shock. There were multiple minor cuts and abrasions and a considerable scalp wound, which had been sutured. The pulse rate was increased and the temperature elevated, and the pulse beat was of poor quality. The right side of the abdomen was rigid over the lower half with generalized distention and tympanites. The scrotum was hemorrhagic, and the size of a large grapefruit, there was a large scrotal hernia on the right. A wide defect was present to palpation at the symphysis. There was great tenderness over the lumbosacral and right sacro-iliac joints, and pressure anywhere on the pelvis was painful. There seemed to be gross abnormal mobility of the right innominate bone with considerable cephalad displacement. The patient had not voided spontaneously, and the urine had been bloody on each catheterization.

A roentgen examination was made on admission. At this time glass plates were being used, which have not been preserved. The detailed report is as follows: "There is a fracture of the right transverse process of the fifth lumbar vertebra with 1 inch upward displacement. There is a dislocation of the sacro-iliac synchondrosis on the right, the ilium being displaced upward about 1 inch, with  $\frac{1}{2}$  inch separation of joint surfaces. There is a complete dislocation of the symphysis pubis with 2 inch separation. There is a fracture of the ascending ramus on the right side of the pubis with no displacement and a comminuted fracture of the descending ramus, one fracture line being near the pubis and the other near the ischium, the fragment being displaced considerably downward and backward."

The patient was placed on a Bradford frame and in addition a canvas hammock-sling with overhead suspension to the pelvis were used. Adhesive traction was applied to the right lower extremity with about 30 pounds weight and elevation of the foot of the bed. Supportive treatment was pushed, and a retention catheter was inserted.

Following these measures there was some improvement in comfort and general condition, and no definite evidence of peritonitis obtained. However, tympanites increased, and a paralytic ileus seemed imminent, only most energetic nursing, with administration of stupes and solution of pituitary finally starting intestinal elimination. It was ten days after admission, however, before this condition was entirely controlled. The principal complaint during this period was intense sciatica on the right side, which resisted the heaviest doses of narcotics and sedatives. A considerable traumatic psychosis prevailed for many days, and the patient absolutely would not tolerate the weight extension, which had to be removed after a few days. Bronchitis was noted a few days after admission and became rather diffuse, but inhalations and the use of blow bottles was pushed, and consolidation did not develop. However, there was indication of a migratory bronchopneumonia



Fig 1 (case 2) —Roentgenogram made five years after injury. No disability referable to the pelvis. The original roentgenogram of this case made on glass plates was not preserved. See roentgen interpretation in the text. First examination showed 1 inch upward displacement of the innominate at the right sacro-iliac joint and 2 inch separation at the symphysis. Note the fusion of the right sacro-iliac with little residual displacement. Originals of this print show some bony continuity across the front of the pelvis, not obvious in the print.

with fluctuating temperature and respiration prevailing for the first four weeks. For the first two weeks, the temperature ranged from 99.5 to 103 F. and in the ensuing fortnight between normal and 101 F. The pulse rate followed the temperature, ranging between 100 and 120. During most of this period the patient was on critical list.

One month after admission, clinically there seemed to be persisting innominate dislocation and a continued complaint of sciatic pain. A portable x-ray apparatus was not then available, and it had not been felt safe to move the patient

On the thirtieth day after admission, his general condition being fairly satisfactory and the condition of the chest clearing up, he was sent for further roentgen examination, being moved on a Bradford frame with a canvas corset to the pelvis. Roentgenograms showed little change, save for some decrease in the pubic separation.

The patient and his family were then told that without operation there would probably be continued pain, disability and invalidism, but that operation entailed considerable inevitable risk. It was decided to accept this risk, however, and at the end of the fifth week, closed reduction was performed under ether. The method was that described elsewhere in this article.

Postoperative convalescence was unexpectedly good, no pulmonary complications following. A cast was applied, making it possible to turn the patient completely over, which helped in this connection. On the other hand, the tendency to distention recurred about a week after operation, and continued to be a problem until the cast was removed at the end of three weeks. Four weeks after operation he began to sit up in bed, and two weeks later in a wheel chair, with a webbing belt. An annoying complication about this time was a severe edema of the lower extremities, without nephritic symptoms, on the right side, the edema almost had the aspects of an elephantiasis. It was followed by severe arthritic disturbances in all these joints that proved extremely resistant to physical therapeutic measures. Three months after reduction and four months after admission, the patient began to use crutches, but he did not leave the hospital for another month.

The postoperative and final roentgen examinations showed fairly complete reposition of the right innominate bone.

The patient did not report again for four months, at which time he was still using crutches but was able to walk about the room easily without them. He laid his difficulty to stiffness and weakness of the knees and ankles. Bony relations at the symphysis and sacro-iliac joints seemed normal, and manipulative tests were negative. There was considerable limitation of motion of the lower part of the back. Nine months after injury he was getting about more comfortably with a cane, and the joints were less swollen and their movements less limited. He reported occasional attacks of mild sciatic pain. No further observations were obtained at that time, but friends reported a year later that he had gone back to work.

Recently he returned for repair of a scrotal hernia. Considerable disability had persisted from arthritic symptoms in the knees, ankles and feet, but he had no symptoms referable to the pelvis. He was able to walk moderate distances, using a cane on account of lameness in the knees. He could bear his entire weight on either limb without any discomfort around the pelvis. There was considerable limitation of motion of the lumbar spine, but no further complaint of sciatica. No mobility at the symphysis could be made out on manipulation. Roentgenograms obtained at this time are here shown.

CASE 3—James H., a truck driver, aged 31, on April 20, 1924, was caught between his machine and a moving freight car with injuries to the region of the pelvis. He was rendered helpless and brought to the hospital by ambulance about one and one-half hours after the accident. On admission, he was in a state of moderate shock but he rallied very quickly. He complained of great pain in the low part of the back and in the front part of the pelvis which was increased by any pressure on the pelvis or movement of the hips. He was unable to move either hip actively. There were great tenderness and some deformity in the pubic region. There was a definite left inguinal hernia on long standing. The patient was placed on a Bradford frame with pelvic swathe and given moderate supportive treatment.



Roentgenograms then obtained showed slight separation without displacement of the pubis and a longitudinal fracture through the body of the right pubic bone with 1 inch separation, an oblique fracture across the body of the right ilium, and moderate separation of the right-sacro-iliac joint, fractures of both rami of the left pubic bone near the symphysis, with slight separation, marked separation and dislocation of the left sacro-iliac joint

He voided normally during the night without blood in the urine, and no complications developed in the ensuing days. On the fourth day after admission closed reduction was performed under ether anesthesia. The method described elsewhere was again used, and it is of importance to note that with removal of the binder and manipulation of the pelvis, a much wider separation of the pubis became palpable and was fluoroscopically observed than was apparent in the original x-ray films taken after the frame and swathe had been applied. The separation of the right sacro-iliac joint did not seem to be accompanied by any displacement, and manipulation was confined to reduction of the displaced right innominate bone.

When the patient was returned to his room, the foot of the bed being elevated, adhesive traction was applied to both lower extremities, with a 20 pound pull on each leg. A hammock sling was placed around the pelvis with overhead suspension of the same amount. No complications followed the operation, and the patient reported complete relief from pain.

Traction on the legs was gradually decreased after the first week and discontinued at the end of the four weeks, reduction being maintained by the hammock suspension. This was discontinued at the tenth week, a webbing belt being substituted, and the patient started to sit up in bed. He was allowed in a wheel chair in the twelfth week and on crutches soon after. He was walking the length of the corridor without discomfort four months after the injury. Discharge was authorized at this time, but the patient elected to have an operation for hernia before leaving, and was transferred to the department of general surgery for that purpose, leaving the hospital three weeks later.

This man proved rather slow in returning to work, which he did not do until six months later, he complained a good deal during that period of symptoms of vasomotor disturbance in the right foot and leg. This responded gradually to physical therapy. One year after the accident, while still holding a light job, he was reported as covering a golf course without symptoms on holidays, and he was put back on full duty. Everything was satisfactory until eighteen months after the injury, when he returned with symptoms of lumbar arthritis. These cleared up when some severe oral sepsis was cared for. Roentgenograms obtained one year after injury showed definite fusion of the left sacro-iliac joint and suggestive fusion of the right joint.

CASE 4—George R., a French-Canadian laborer, aged 18, of slight build, on May 3, 1926, fell 125 feet from a scaffold. Near the ground the boards of a light staging broke the full force of his fall as he crashed through them to the concrete surface below. He reached the hospital in fifteen or twenty minutes. He was unconscious on arrival, and was stuporous for forty-eight hours. No signs of fracture of the skull appeared, but he was in an extreme condition of shock. On admission, blood pressure was 60 systolic. Obvious disalignment of the pelvis led to immediate fixation with the binder and Bradford frame without more detailed local examination. There were abrasions but no lacerations and no definite evidence of visceral injury, though the abdomen was very rigid in the lower half. This, however, led to catheterization as there was a possibility of a ruptured bladder. Three hundred cubic centimeters of clear urine was obtained, followed by 20 cc of blood. A retention catheter was not thought to be indicated.



Fig 2 (case 3) —Original roentgenogram made after fixation on a Bradford frame plus a pelvic swathe. Note the upward displacement of the left innominate, and fracture of the left ramus and right pubic body.

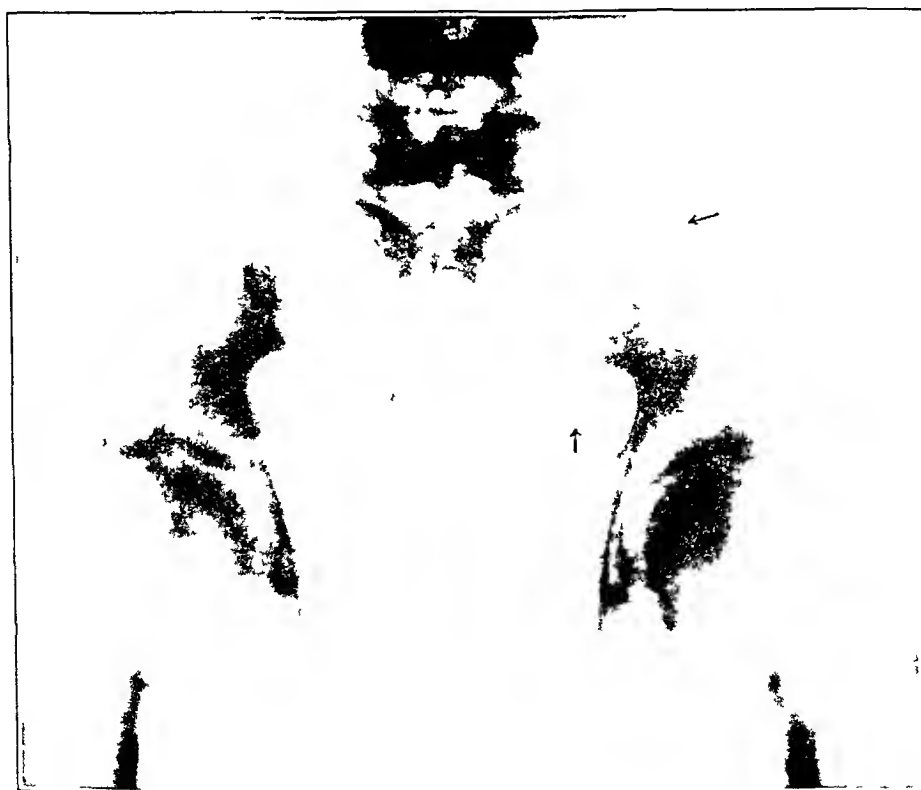


Fig 3 (case 3) —Roentgenogram showing the end-result with no residual disability. Note the fusion of the left sacro-iliac with but slight displacement also the consolidation in front.

The condition of shock resisted most vigorous measures for the first twelve hours. Except after the administration of saline intravenously or after epinephrine, the systolic pressure was between 60 and 75 or was not obtainable. Hypodermoclysis with frequent small doses of caffeine finally seemed most effective and kept the pressure fairly steady around 100 by the end of twelve hours, and at the end of twenty-four hours the quality of the pulse was good, with a pressure of 120 systolic and 80 diastolic.

Roentgen examination showed a severe upward dislocation of the left innominate bone, there being great separation in front in spite of the binder, and in addition a horizontal fracture across the body of the right ilium between the



Fig. 4 (case 4)—Roentgenogram showing patient's condition on admission. Slight separation of the left sacro-iliac joint, marked separation and displacement of the right sacro-iliac joint, marked separation and displacement of the symphysis and pubis, upward and outward dislocation of the right innominate bone,  $1\frac{1}{2}$  inches at the back and 2 inches at the front and linear fracture across the body of the ilium are noted.

sacrosciatic notch and the anterior superior spine, no displacement, however, being present at the site of fracture.

The patient's condition of shock rapidly changed to one of extreme traumatic psychosis, so that he was either irrational or delirious and required restraint for the first few days. Although the urine became clear after the first day, voiding was not spontaneous until the third day. On the fourth day, tympanites became extreme, and he seemed dangerously toxic, but this condition finally responded to stupes, enemas and a solution of pituitary. During this period the temperature

ranged between 102 and 103 F, and the pulse rate between 120 and 130. On the sixth day, both were slightly lower, and he did not seem at all toxic, though still irrational.

It was then felt that the persisting innominate displacement was a factor in continuing both the organic and the mental disturbances, and reduction under anesthetic was accordingly carried out. The method elsewhere described was again used, and the immediate fluoroscopic control suggested practically complete reposition.

After reduction, improvement in the condition became rapid in every respect. Only one catheterization was required. The patient seemed to have less pain, he



Fig 5 (case 4) —Pelvis after reduction by closed methods. Upward displacement in the right sacro-iliac is almost completely reduced, but rotation is not completely corrected as evidenced by the level of the pubic bones. There is incomplete reduction of the separation of the symphysis.

was easily managed, and his mental condition became steadily better, though he was not completely cooperative for another week. The traction on the leg and the hammock sling were continued. Bedside films two weeks after reduction, which to clinical examination still seemed complete, showed that there was a rotation or eversion deformity and slight separation persisting at the symphysis. A webbing buckled binder was substituted for the hammock sling but though constantly tightened films after another two weeks showed little change. It was felt that wiring was indicated on this account but this procedure was deferred until after a cystitis cleared up in the seventh week. Operation was performed on June 23, under ethylene. It was found that even after the bladder and urethra

were freed and the pubic space thoroughly cleared between the two bones, even with maximum contralateral traction on heavy wires passed around each pubic bone, little further apposition could be obtained. The pelvic ring seemed to be solid at the back. The symphysis was wired in the best possible position, and an osteoplastic bridge made across the pubic spines.

Postoperative treatment was by frame and belt. Convalescence was entirely uncomplicated. The patient sat up in bed two weeks after operation and two months after the accident. He was up in a chair a few days later, and on crutches three weeks after operation. At the time of discharge, two days later, he was walking unaided and without limping. There were no shortening and no palpable mobility at the symphysis.



Fig 6 (case 4) —Roentgenograms showing the end-result four months after wiring, the patient is back at work as a structural iron worker, with no residual disability or complaint. Asymmetry of the pelvis is due partly to the position of the patient, but mostly to an incomplete correction of the rotation deformity. Note the fusion of the sacro-iliac in normal position and the acetabula at the same level. The symphysis pubis is fused by a bony bridge residual from a light graft not clearly shown in the print. An interesting bridging of the lateral process of the fifth lumbar to the right ilium seems to be causing no disability.

The patient was reexamined four months later, about six months after injury, and voluntarily demonstrated his recovery by standing up on a table and jumping down to the floor. His posture showed no list, mobility of the spine was complete, Trendelenberg's sign was negative, and there was no mobility or apparent discomfort on any manipulation of the pelvis. Roentgenograms then obtained and produced here show a bony bridge at the site of the osteoplastic grafts across the symphysis.

CASE 5—J. P., a mechanic aged 40, was admitted to the hospital on Dec 7, 1926 after a crushing blow on the right side of the pelvis. On admission, he was in a rather marked state of shock with bleeding from the urethra. A retention catheter was inserted and stimulative treatment in the first twenty-four hours brought considerable improvement. On the second day, symptoms of peritonitis rapidly progressed and laparotomy was done on the supposition that the bladder was ruptured. At operation no bladder or other visceral or parietal peritoneal damage was present. There was however some free blood-tinged fluid and an extensive rent through a segment of mesentery of the ileum, the vessels of which were thromboid and not bleeding, but the corresponding bowel, for about 18 inches, was deprived of its blood supply and was gangrenous. This loop was brought



Fig 7 (case 5) —An acute pelvic injury apparently comparable to the preceding illustration but really not containing any true dislocation either front or back, but instead a rather unusual vertical fracture through the sacrum just mesial to the sacro-iliac joint with multiple fractures of the front of the pelvis. Note the great upward displacement of the innominate. The patient was injured by being squeezed and rolled between heavy moving objects. There was a fatal and rather unusual internal abdominal injury, extensive laceration of the mesentery of the small intestine with very little hemorrhage but with progressive thrombosis and intestinal gangrene.

outside of the abdomen for Mikulicz' enterostomy, being opened and drained through both loops twelve hours later. Considerable improvement followed for a few days, when signs of progressive peritonitis again supervened. The patient died on the sixth day after injury. A roentgenogram showed (fig 7) tremendous upward displacement of one innominate bone.



Fig 11 (case 8) —Condition on admission Note fracture dislocation of left sacro-iliac joint, rupture of symphysis pubis and upward displacement of left innominate bone, also fracture in lateral processes of lumbar vertebrae

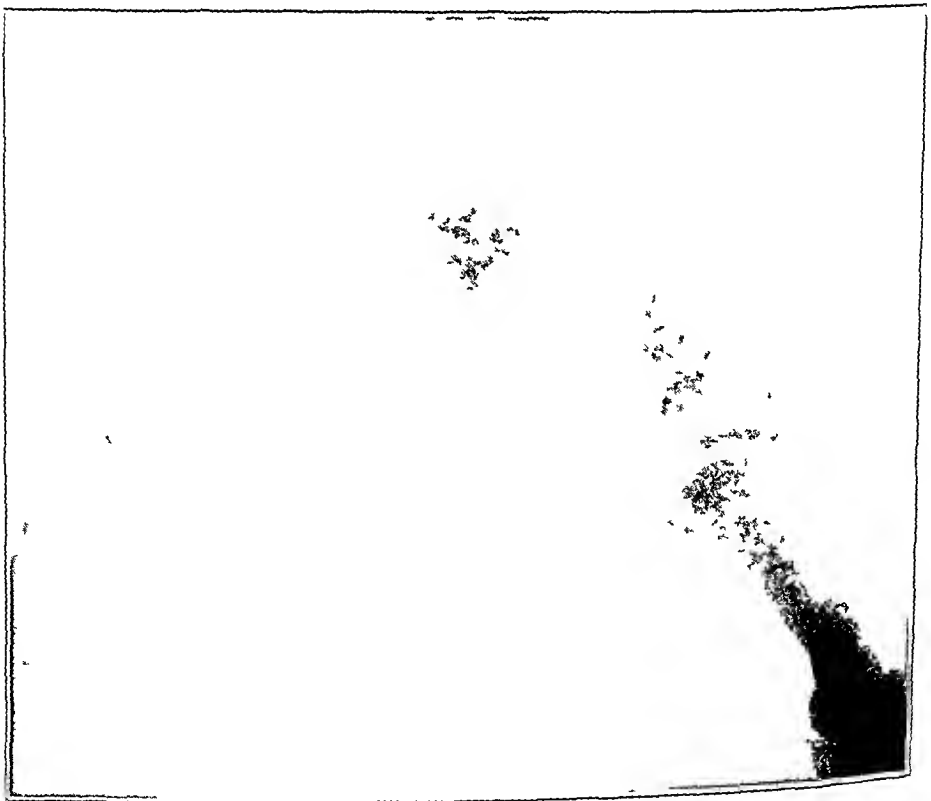


Fig 12 (case 8) —Roentgenogram showing reduction of sacro-iliac fracture and correction of upward displacement of innominate bone secured by simple traction without manipulation Following examination, a pelvic hammock sling was added but before illustration was made traction was discontinued to transfer the patient

luxation of the right innominate bone with an oblique fracture through the ilium running into the sacro-iliac synchondrosis. The innominate bone was displaced slightly posteriorly and at front also medially so that the two pubic bones completely overlapped.

As bloody urine was obtained a diagnosis of injury to the bladder seemed probable during the day dullness developed in the lower part of the abdomen and also projectile vomiting leading to laparotomy about eight hours after admission. At operation laceration of the bladder was found slightly to the left just above the urethra. This was closed with cystostomy and drainage of the prevesical space. Transfusion was given following operation. The patient improved considerably at first but a progressive and critical ileus led to enterostomy on the

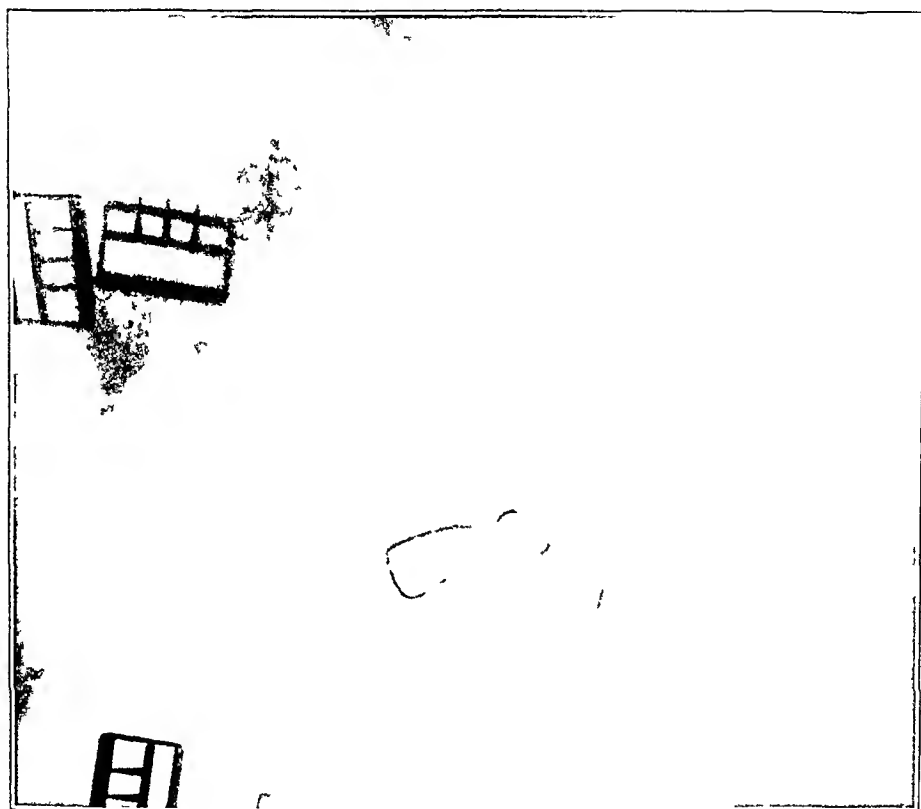


Fig. 13 (case 8)—Usual manipulative technique having failed to correct the recurrence of some upward displacement and rotation of the left innominate, apposition and consolidation of the pubis in front was obtained by wiring with plastic osteotomy of the left pubic bone. Some bony callus can be seen around the lower pole of the left sacro-iliac. This patient was returned to full duty as a machinist

following day. The distention was gradually overcome, but the patient continued to be quite ill for a long time, with evidence of septic complications. A history of a preceding chronic cystitis and pyelitis with obviously infected bladder combined with his injuries to make the course a stormy one. Osteomyelitis of the pubic bones developed from the local infection. The fecal fistula was very slow to close. Healing of the suprapubic sinus finally occurred at the end of about four months, and of the fecal fistula about two weeks later.



On account of the injury to the bladder the patient had been transferred to the urological division for operation. Operation verified the roentgen observations as to the position of the pubic bones at the time of cystotomy. No definite manipulative procedures aiming toward reduction were carried out, but the patient was placed on a fracture bed with the body supported on slings, on account of the handling of the indwelling catheter, his legs were left considerably abducted. His condition was such that for many weeks any intervention or manipulation for the skeletal injury was safe. About four weeks after admission, portable films were obtained which showed the relations of the two halves of the pelvis to be normal save for an increased space at the symphysis pubis. There also was evidence of



Fig 14 (case 4) —Illustrating technic of closed reduction for innominate displacement. The patient is on a tilting fluoroscopic table hanging suspended by the foot of the displaced side, while counter rotation of the rest of the pelvis is performed by straight leg manipulation on the other side. The assistant steadies the pelvis and verifies the movement of the pubic bones, which is then followed by fluoroscopic check. See details in text.

osteomyelitis of the left pubic bone. Subsequent roentgenograms showed no further change in relations and evidence of healing of the bone infection. Seven months after injury the pelvis seemed solid on examination and the patient began to sit up, but he did not walk until after another four months. At that time no symptoms referable to skeletal injury prevailed.

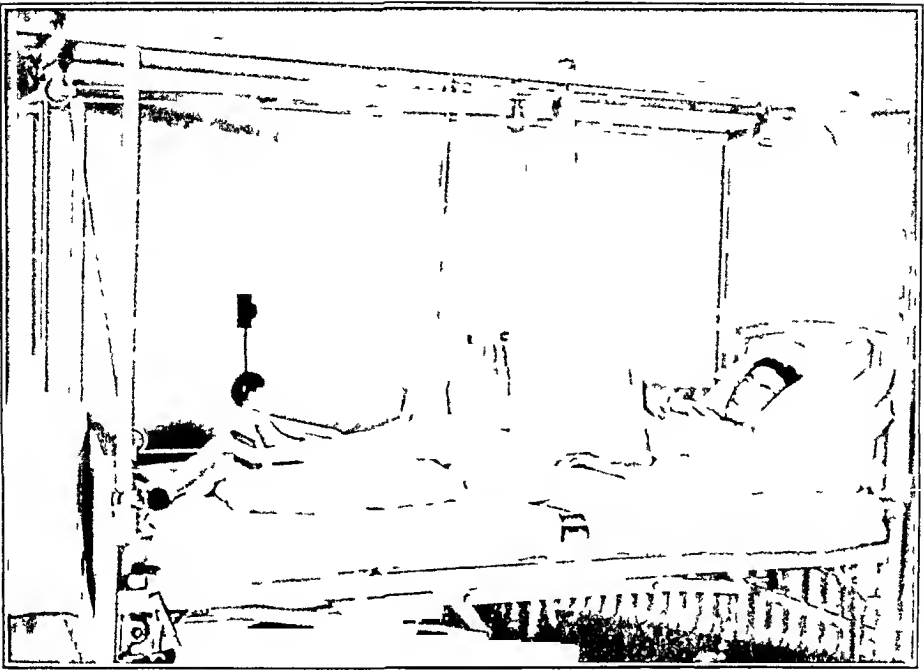


Fig 15 (case 4) —Method of retention of reduction during convalescence by pelvic suspension and longitudinal traction on the displaced side

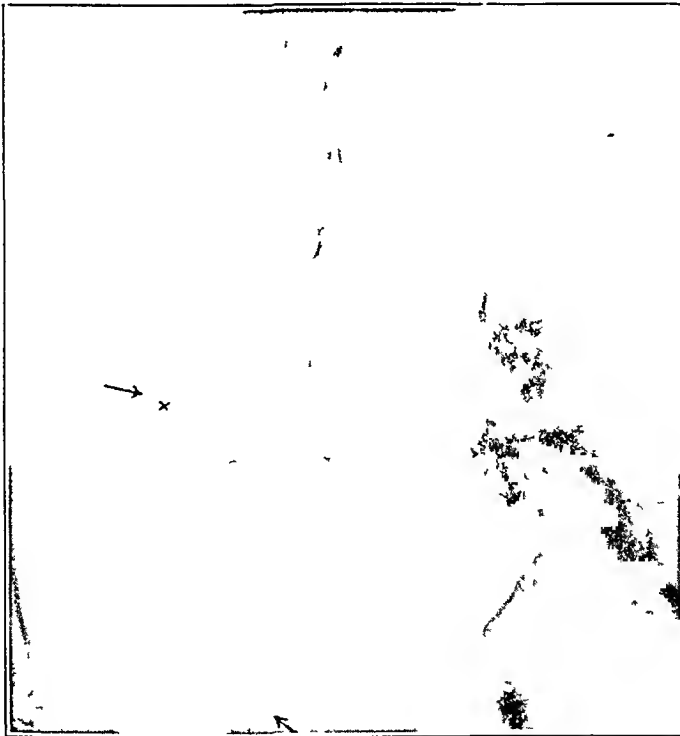


Fig 16—Roentgenogram from an old case lately discovered in the files, after the patient was examined for a back complaint. The injury occurred ten years previously with recovery after six months. There was persistent low back pain which spread upward, a clinical diagnosis of ankylosing spondylitis was corroborated by a roentgenogram. See also the difference in the level of the iliac crest and derangement of the symphysis. Roentgenogram taken to show condition of spine.

CASE 8—J B, a mechanic aged 26, was admitted to the hospital in the morning of Dec 8, 1927 a few minutes after an automobile accident in which his car overturned, but the mechanism of the injury was not further recalled. He showed laceration over the right eye, bruises around the trunk and legs, crepitation and severe localized tenderness over the left posterior iliac crest, hypermobility of the pelvis in front, with extreme pain on handling. Roentgenograms showed an upward luxation of the left innominate bone both pubic and sacro-iliac syndesmoses being ruptured, a fracture with slight displacement through the posterior part of the left ilium and fractures of the left lateral processes of the third, fourth and fifth lumbar vertebrae. Roentgenograms of the skull were negative.

The patient was placed on a Bradford frame and general supportive measures were instituted. During the day he developed rather marked symptoms of shock, which, however, responded to a second intravenous infusion of dextrose. There were also several attacks of vomiting, but only after ingestion. As considerable abdominal tenderness developed, with continued inability to void, catheterization was done, but the urine was clear. During the first few days the patient was at times stuporous or irrational, but no other or further evidence of cerebral injury developed. On the second day, longitudinal traction of 25 pounds on the leg of the displaced side was begun on a fracture bed but no more vigorous measures of reduction seemed safe in view of his general condition.

At the end of a week, the patient's general condition was very good but although no wound or external evidence of trauma had been observed a rather marked parotitis, with considerable elevation of temperature, developed. This responded to conservative measures, but was responsible for further postponement of manipulative treatment of the pelvic displacement. However, roentgen examination made with a portable x-ray apparatus on the thirteenth day, showed apparently complete correction of the upward displacement of the left innominate bone. Traction was therefore discontinued in favor of a pelvic hammock to accomplish reduction of the separation of the symphysis. It was about ten days later that transfer to another building had to be made, and by some oversight, the next examination did not occur until four weeks after admission, when some recurrence of upward displacement with an additional rotation deformity was observed.

Manipulation under the fluoroscope by the technic described was at once carried out, and it was thought that considerable improvement in position was obtained. However, control roentgenograms subsequently showed imperfect apposition with overlapping of the pubic bones in front. Open reduction, with an osteoplasty of the left pubis and wiring, was accordingly performed about six weeks after admission. External fixation after operation was continued in a double plaster spica. Convalescence was uncomplicated, and the roentgenogram showed an apparently satisfactory result. It should be noted that at operation no mobility of the pelvis at the back could be obtained, so that plastic procedure was resorted to to accomplish pubic consolidation. In spite of some persisting rotation of this side of the pelvis, the two acetabula appear at the same level, and there is no clinical shortening of the extremity. The patient has returned to full duty with no complaints.

# CONTRACTURE RESULTING FROM TENOTOMY\*

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The term contracture is used to designate prolonged or more or less permanent muscle shortening. The delayed relaxation seen in a nerve-muscle preparation after a series of rapidly repeated contractions, the delayed relaxation caused by veratrine poisoning, the prolonged shortening caused by nicotine and acetylcholine in frog muscle and in denervated mammalian muscle and Tigel's contracture are chiefly of interest to the physiologist. With the exception of the first mentioned which is generally regarded as a fatigue contracture due to the accumulation of lactic acid in the muscle, not much is known about the physico-chemical factors involved in these phenomena. Nor are the structural factors any better understood. The relative parts played by the myofibrils and sarcoplasm are still matters of controversy. In a recent article, Gasser<sup>1</sup> has presented a comprehensive review of the various types of contracture with which the physiologist is familiar and states that these are of an entirely different nature from the myostatic contractures with which this paper deals.

As ordinarily used in clinical literature, contracture designates a condition of persistent tonic shortening of muscles which will, however, relax during sleep or under anesthesia. To this class belong the contractures seen in some patients with lesions of the pyramidal tract. This sort of muscle shortening is maintained by a continuous stream of nerve impulses reaching the muscles from the central nervous system and affecting one group of muscles predominantly or to the complete exclusion of their antagonists. It is in fact, nothing but an exaggerated and continuous state of hypertonus and is characterized by the deformity which it produces, by its steady persistence during the waking hours, and by the fact that it disappears during deep sleep or anesthesia.<sup>2</sup> Hysterical contracture and the reflex contractures, so often seen during the war, which bear some obscure relation to more or less trifling wounds, also have as their basis an excessive and continuous tonic innervation of the affected muscles. Muscle shortenings of this sort

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\* Submitted for publication April 28, 1930.

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1. Gasser, H. S. Contractures of Skeletal Muscle. *Physiol. Rev.* **10**: 35, 1930.

2. Oppenheim, H. *Textbook of Nervous Diseases*. Edinburgh: O. Schulze & Co., 1911.

whatever their cause, fall in one great group and may properly be designated as hypertonic contractures.

Apparently even in contractures of pyramidal origin there may develop some intrinsic shortening in the muscles, for according to Foerster,<sup>3</sup> while these contractures are due in large part to hypertonus, they are also in part due to the fact that each muscle group adapts itself to the approximating of its points of insertion by the gradual development of contraction and permanently retains this condition of shortening. If this actually occurs, the affected muscles should not fully relax under an anesthetic, and the residual shortening that persisted under deep anesthesia would belong in the class to be described next.

Under the general heading of myostatic contractures have been included a group quite different from the preceding (Ranson and Sams<sup>4</sup>). It includes all contractures that are caused by the fixation of the muscle at a given length for a considerable period of time. Familiar examples are the contractures that restrict the movements of joints after immobilization for weeks in plaster casts, the permanent shortening of muscles after division of their tendons, and probably, in their early stages at least, the paralytic contractures due to the unequal paralysis of antagonistic muscle groups in anterior poliomyelitis and multiple neuritis. Since they all are caused by fixation of the muscle for a long time at one unchanging length, this group of contractures might not improperly be designated as immobilization contractures, but the term myostatic more accurately describes the condition.

By myostatic contracture we mean to designate a condition of permanent shortening in resting muscle which is maintained in the entire absence of nerve impulses, the muscle having acquired, usually as a result of prolonged immobility, a new and shorter resting length. It is the condition which has been designated "Ruheversteifung" by Spiegel and Shiboya.<sup>5</sup> These investigators and others as far back as 1886 (Moll<sup>6</sup>) have clearly demonstrated that if the bony attachments of a skeletal muscle are immobilized for several days so as to prevent the changes in length that normally result from spontaneous and reflex movements, there occurs a fixation of the muscle at the

3 Foerster, O. *Die Kontrakturen bei den Erkrankungen der Pyramidenbahn*, Berlin, S. Karger, 1906.

4 Ranson, S. W., and Sams, C. F. A Study of Muscle in Contracture. The Permanent Shortening of Muscles Caused by Tenotomy and Tetanus Toxin, *J. Neurol. & Psychopath.* **8**: 304, 1928.

5 Spiegel, E. A., and Shiboya, H. Die Bedeutung des Zentralnervensystems für die Entstehung muskularer Contracturen an eingegipften Extremitäten, *Ztschr. f. d. ges. Exper. Med.* **44**: 729, 1928.

6 Moll, A. Experimentelle Untersuchungen über den anatomischen Zustand der Gelenke bei andauernder Immobilization derselben, *Virchows Arch. f. path. Anat.* **105**: 466, 1886.

length thus imposed on it. If taken sufficiently early, this contracture can be overcome by active or passive movements, but if it is left untreated for some time the damage becomes irreparable.

It may be that adhesions and ankylosis play a part in the limitation of motion in a joint that has been enclosed for weeks in a plaster cast, but these factors are certainly secondary to the shortening of the muscles. This is clearly shown by the following experiment (Moll<sup>6</sup>). After the hind leg of a rabbit had been enclosed in a plaster cast for twelve days, division of the muscles completely eliminated all of the resistance to passive movement which had developed. This showed that within this time no adhesions, thickenings of the joint capsule or changes in the articular surfaces had developed and that the limitation of movement was entirely due to a shortening and fixation of the muscles.

Frohlich and Meyer<sup>7</sup> have shown that this fixation of an immobilized muscle is dependent on the nerve impulses that reach it from the central nervous system. Immobilization of a denervated muscle does not cause it to become set or alter its extensibility as would be the case if the nerve supply were intact. According to these authors, section of the dorsal roots supplying the muscle is sufficient to prevent the contracture, indicating that the integrity of the local reflex arc is essential for its development.

Spiegel and Shibuya<sup>8</sup> removed the left motor cortex from cats and found that in the right hind leg the extensor muscles became set more quickly than the flexors, while flexor rigidity was more easily induced on the left side. They carried out other experiments, transecting the spinal cord in the lower thoracic region and then putting the limbs up in plaster casts in the flexed position, and found that setting occurred in the fore limb more quickly than in the hind limb. These experiments indicate that the brain centers that control tonic innervation of the muscles play an important part in the genesis of this phenomenon.

Myostatic contracture is then the fixation or setting of an immobilized muscle in a new and shorter than normal resting length. In its genesis it is dependent on the nervous system and it is probably an abnormal manifestation of tonic innervation. It is, however, only in its genesis that myostatic contracture is dependent on the nervous system. After it has once developed, it is independent of the innervation and persists under deep anesthesia and even after section of the motor nerve. It is a contracture of muscle at rest and is in this respect to be sharply distinguished from the hypertonic contractures previously mentioned.

<sup>7</sup> Frohlich, A. and Meyer, H. H. Untersuchungen über den Tetanus. Arch. exper. Path. u. Pharmacol. **79**: 55, 1916.

Many of the attempts at explanation of contractures of various types have dealt with the hypertonic forms, and a number of the papers have been for the most part reviews of the literature on the controversial questions of muscle tonus. The papers of Buscaino,<sup>8</sup> Cooper,<sup>9</sup> Crocq,<sup>10</sup> Noica,<sup>11</sup> Pieron,<sup>12</sup> and Ott<sup>13</sup> contribute nothing of importance to the problem. Probably the most significant single observation is that attributed by Oppenheim<sup>2</sup> to Brissaud, namely, that an anemia of the affected extremity produced by an Esmaich bandage has a relaxing effect on the shortened muscles. It suggests that the shortened state is not maintained by structural alterations in the muscle, but by a chemicophysical equilibrium that is upset by the anemia.

Ranson and Sams'<sup>4</sup> study of myostatic contractures produced by tetanus toxin and by section of the tendo achillis in rats and cats dealt with the capacity for shortening that the gastrocnemii of these animals retained in their shortened state and the speed of relaxation from nerve-muscle tetanus.

Kymograph records showed that a muscle in myostatic contracture cannot shorten so much as a normal muscle during nerve-muscle tetanus. In these experiments the average normal shortening of the rat's gastrocnemius during contraction was found to be 7.5 mm, and this was reduced to an average of 4.6 mm for the muscles in contracture. While the capacity for shortening during nerve-muscle tetanus was decreased to the same extent in both types of experimental myostatic contracture, the rate of relaxation was unaffected by tenotomy but was considerably reduced by tetanus toxin.

The height of contraction and the rate of relaxation of a muscle in tetanus contracture were the same whether the muscle was stimulated directly or through its nerve. This showed that the defective contraction cannot be explained on the basis of an involvement of the nerve or nerve endings.

Changes in length of the muscles and of individual fibers and changes in weight were also noted. In both tetanus contracture and that following tenotomy, fibers in the cat's and rat's gastrocnemius had

8 Buscaino, V. M. Genesi tossica della contrattura, esperimenti e critiche, Riv di pat nerv **17** 330, 1912.

9 Cooper, G. Contractures and Allied Conditions. Brit M J **1** 109, 1917.

10 Crocq, J. Le mecanisme du tonus musculaire des reflexes et de la contracture, Encephale **9** 147 and 197, 1914.

11 Noica, M. Le mecanisme de la contracture spasmodique. Presse med **19** 153, 1911.

12 Pieron, H. Du mecanisme physiologique du tonus musculaire comme introduction a la theorie des contractures, Presse med **26** 88, 1918.

13 Ott, A. Considerazioni sulla fisiopatologia della contrattura, Riv di pat nerv **17** 429, 1913.

become permanently shortened 45 or 50 per cent of their normal length but owing to the obliquity of the fibers the muscle as a whole underwent a shortening of only 10 or 12 per cent. The weight of the muscle remained normal in tetanus contracture but after tenotomy there was an average loss of weight of 18 per cent.

Davenport Davenport and Ranson<sup>14</sup> have found that the lactic acid content of rabbit and guinea-pig muscles in the contracture caused by tetanus toxin is within the same range as that of normal muscles either from the unaffected side of the same animal or from normal animals. The glycogen content<sup>1</sup> of guinea-pig and rabbit gastrocnemii is usually reduced during the early stages of the contracture while it is still dependent on innervation. Rats show little change in glycogen content at the same period. In later stages of tetanus contracture the glycogen content of contracted and normal sides is usually about the same, though frequently both are lower than in normal animals. The glycogen content seems to bear no causative relationship to contracture. Wertheimer's<sup>16</sup> experiments led him to believe likewise that glycogen change had little to do with contracture. Determinations of changes in acid-soluble phosphorus fractions in rabbit muscles in tetanus contracture<sup>17</sup> showed an apparent reduction in the total quantity and a similar decrease in phosphocreatine. Determination of protein nitrogen in these muscles indicated that the water content of the muscle in tetanus contracture was greater than that of the normal. The decrease in total phosphorus was proportional to the increase in water in the muscle and the decrease in phosphocreatine was only a little greater than could be accounted for by the change in water content. Since tetanus muscles are more brittle than normal ones, stimulation occurring during freezing may have been responsible for the reduction of phosphocreatine. It is believed that there was no significant change in absolute quantities of acid-soluble phosphorus fractions since the remaining fractions varied inconstantly. The fat content in tetanus muscles of rabbits was 10 per cent greater in three of five animals and in the other two it was the same as the normal muscles.

14 Davenport, H. A., Davenport, H. K., and Ranson, S. W. Chemical Studies of Muscle Contracture. I. The Lactic Acid Content, *J. Biol. Chem.* **79** 499, 1928.

15 Davenport, H. A., Davenport, H. K., and Ranson, S. W. Chemical Studies of Muscle Contracture. III. The Change in Glycogen During Shortening Produced by Tetanus Toxin, *J. Biol. Chem.* **82** 499, 1929.

16 Wertheimer, E. Verändert sich der Glykogenbestand bei der tonischen Contractur quergestreifter Muskeln, *Arch. f. d. ges. Physiol.* **221** 139, 1929.

17 Davenport, H. A., Davenport, H. K., and Ranson, S. W. Chemical Studies of Muscle Contracture. IV. Changes in Phosphorus, Nitrogen and Fat Content During Shortening Produced by Tetanus Toxin, *J. Biol. Chem.* **87** 295, 1930.



Experimental work on changes in structure of skeletal muscle in various stages of contraction and kinds of contracture has been done by Frank<sup>18</sup>. He determined by measurement of the cross-striations the relationships between the widths of isotropic and anisotropic bands in isometric contraction, stretched isometric contraction, stretched resting muscle, fatigue contracture, chloroform contracture and rigor mortis. He found the ratio of the width of isotropic to anisotropic bands the same in chloroform contracture, rigor mortis, resting muscle and in complete fatigue. This was different, however, from the ratio found in varying degrees of contraction. He believed therefore that true contractions and contractures of various kinds are not of the same nature.

Hurthle's<sup>19</sup> recent experiments on frog muscle were undertaken because Frank's work on frog muscle disagreed with work which Hurthle had done on *Hydriophylus* muscle. Hurthle investigated the effects of chemical fixation on the maintenance of contraction produced by electrical stimulation. His use of kymograph tracings made during fixation of the muscle while it was being stimulated showed some differences in response to various fixatives and a partial relaxation of the muscle from the initial contraction induced by the fixative, which Frank believed augmented that caused by electrical stimulation. He was able to obtain the same histologic picture that Frank did when his material was handled in the same way, but in view of the variation caused by different methods of handling, he did not feel that such a picture could be taken as the true condition of living muscle.

Nageotte<sup>20</sup> studied the microscopic changes in frog muscles in the extreme contracture produced by faradic stimulation and that produced by exposure to strong chloroform vapors.<sup>21</sup> He obtained fibers presenting under the microscope a mottled appearance, which he interpreted as contraction of the myofibrils in spots since it could be prevented if the muscle were pulled out slightly before fixation. The early stages of chloroform contracture resembled various stages of faradic contraction and were also reversible so long as the muscle remained elec-

18 Frank, G. Das histologische Bild der Muskelkontraktion. Arch f d ges Physiol **218** 37, 1927.

19 Hurthle, K. Zur Kenntnis der Struktur des ruhenden und des tatigen Froschmuskels. I. Abhandlung. Lässt sich die Struktur des Froschmuskels im Zustand der Verkürzung durch chemische Fixierungsmittel festhalten? Arch f d ges Physiol **223** 685, 1930.

20 Nageotte, J. Sur la contraction extrême du muscle strié chez la grenouille. Compt rend Acad d sc **180** 761, 1925.

21 Nageotte, J. Sur la morphologie du muscle strié en état de contracture chloroformique chez la grenouille. Compt rend Acad d sc **180** 1963, 1925.

tically excitable but in the later irreversible stage when plasma was expelled from the fibers and coagulated on the surface the picture was quite different

Gavrilescu<sup>22</sup> has repeated Nageotte's work on chloroform contracture studying fixed and stained material and, in addition, the fresh, unstained fibers. He confirmed Nageotte's work on the stained material. In the fresh material, however, contraction waves could be seen moving down the fibers when they were exposed to chloroform. The cross-striations were altered in the contracted portion of the fiber as the wave passed along, the dark bands appearing to approach closer to one another so that the contracted part was darkened. The author was unable to say whether there was a reversal of striation. In order to eliminate the chemical factor that might possibly be involved in chloroform contracture, he<sup>23</sup> carried out another series using direct electrical stimulation. Here also he examined both stained and fresh muscle. His observations agreed with those of Nageotte for stimulated muscle on the stained tissue, but in fresh muscle stimulated to contracture and then examined in physiologic solution of sodium chloride, there was no alteration in striation and the fibers appeared normal.

In a note concerning Gavrilescu's work, Nageotte<sup>24</sup> refers to his own work<sup>20</sup> in which he had observed a tendency for the muscles to relax a little spontaneously after cessation of stimulation and in which it was possible to stretch them out to normal length with a little gentle traction. He does not, therefore, believe it possible to dissect off small pieces of fresh muscle from the contracted muscle and maintain extreme contracture.

The microscopic changes occurring in rat's gastrocnemii in contracture produced by tetanus toxin have been studied in this laboratory.<sup>25</sup> The fibers showed more pronounced longitudinal fibrillation and blurred cross-striations. The blurring of the cross-striations was due in part to a loss of alignment of myofibrils and in part to lack of uniformity in reaction to stains in different parts of the fibers. This produced a mottled effect which will be described in more detail later in the paper. Measurements of the width of isotropic and anisotropic bands in regions

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22 Gavrilescu, N. La contracture chloroformique et les modifications de la fibre striée, *Compt rend Soc de biol* **101** 771, 1929.

23 Gavrilescu, N. L'aspect de la fibre musculaire striée lors de la contracture électrique, *Compt rend Soc de biol* **101** 852, 1929.

24 Nageotte, J. Au sujet de l'aspect histologique de la fibre musculaire striée lors de la contracture électrique, *Compt rend Soc de biol* **101** 990, 1929.

25 Davenport, Helen K., Ranson, S. W., and Stevens, E. Microscopic Changes of Muscle in Myostatic Contracture Caused by Tetanus Toxin, *Arch Path* **7** 978 (June) 1929.

taking the stain with different intensity showed that their spacings bore no relation to the intensity with which a given part of a fiber stained, so that the darker color was not due to widening or approximation of anisotropic bands in one region and reversal of the condition or normal spacing in another. Some fibers stained uniformly, but the isotropic bands were narrowed throughout. There was frequently great variation between the appearance of adjacent fibers in the same field. Scattered fibers in some specimens appeared to be undergoing degeneration. There was some increase in sarcolemma nuclei and in the number of large wandering cells. Cross-sections showed an increase in the thickness of the fibers, and measurements showed that they were 23 per cent greater in diameter than the normal fibers. No increase in connective tissue could be seen. Figures for the total shortening of the muscle and for the shortening of individual fibers were found to be about the same as those given by Ranson and Sams for muscle in tetanus contracture. Likewise, there was no decrease in weight in the tetanus muscles. The changes observed did not explain the fixation of the muscle in the shortened state.

The present paper deals with the microscopic changes that take place in the gastrocnemius muscle of white rats, guinea-pigs and cats in which the tendo achillis has been sectioned and makes a comparison of such changes with those already outlined for tetanus contracture.

#### METHOD

Four cats were killed seventeen days, two guinea-pigs and ten rats sixteen days, and three rats forty-four days after section of the tendo achillis in the right leg. The left gastrocnemius served as control. The gastrocnemii were dissected out immediately on the death of the animal. Before removal of the right gastrocnemius from the leg, the distance between the cut ends of the tendon was measured while the ankle was held at a right angle. This was done only on rats. The muscles were then removed and suspended in a moist chamber for one hour under a tension of 50 Gm for rats, 100 Gm for guinea-pigs and 200 Gm for cats, and then placed in fixing fluid with the weight still attached. Fixation and staining methods were the same as those employed in the study of muscle in tetanus contracture, i.e., formaldehyde U.S.P. (1:10), Zenker's fluid and Bouin's fluid for fixation, and for staining, hematoxylin and eosin, iron hematoxylin, van Gieson's picrofuchsin, and Mallory's triple connective tissue stain. All four stains were used after each fixative since the manner of fixation permitted the use of only one fixative on a given animal.

After fixation, the right and left gastrocnemii of each rat were dried off carefully with filter paper and weighed and measured. The total length of the muscle and the length of the fibers in an easily identifiable bundle were measured in both the shortened and control muscles.

Paraffin sections longitudinal and transverse, from 6 to 8 microns thick, were prepared for microscopic study. Sections from both the control and the shortened muscle were mounted on the same slide to insure uniformity of treatment.

## RESULTS

*Gross Changes*—The gastrocnemii of which the achilles tendon had been cut showed the typical picture of contracture. They were short and plump and had pulled the cut ends of the tendon apart. The distance between the cut ends, as measured while the ankle was held at a right angle, varied from 6.5 to 12.8 mm. in rats. The three rats that had been kept for forty-four days after tendon section showed fairly well defined new tendons formed by a filling in of the space between the cut ends of the old one, presumably with connective tissue, though no histologic examination was made of the tissue. Two of these animals had regained the function of their limbs so that there was little difference in the way they used their hind legs. The third rat had regained considerable function also but it was not so nearly normal as the other two. The space between the cut ends of the old tendon was greater in this rat than in the others.

Some atrophy had taken place in our preparations in which the tendon had been sectioned. This was shown by the difference in the weights of the right and left gastrocnemii. The average weight of the shortened muscles of rats was 0.91 Gm. that of the normal muscles, 1.14 Gm. The loss of weight averaged 20 per cent. The shortened muscles of two cats averaged 15.8 Gm., the normal 20 Gm., showing a loss of 21 per cent in weight. The muscles of two of the cats and the guinea-pigs were not weighed or measured but presented the same short, plump appearance as those which were. Audova<sup>26</sup> found in his experiments on rabbits in which the tendo achillis had been cut for from twelve to sixteen days that there was an average loss of weight in the fresh muscle of 19.1 per cent. Lange<sup>27</sup> did some experimental work on rabbits to determine the importance of tension for muscle atrophy and regeneration. He cut the achilles tendon and excised a piece of it together with from one third to one half of the gastrocnemius. In one series of experiments a silk thread was attached to the remaining stump of the gastrocnemius at one end and the calcaneus at the other and drawn as tight as possible without pulling it out of the muscle. Regeneration did not occur after four months. Degeneration was present instead. In another series the thread was adjusted to approximate the normal tension. Here regeneration started from the muscle down over the thread in about eight weeks and after sixteen weeks the preparation had the appearance of normal muscle with normal tendon. In a third series, a connection was made between

<sup>26</sup> Audova, A. Ueber den zeitlichen Verlauf der Muskelatrophie nach Sehnendurchschneidung, Schweiz Arch f Neurol u Psychiat **10** 211 1922

<sup>27</sup> Lange, M. Die Bedeutung der Spannung für die Muskelatrophie und Muskelregeneration. Verhandl d deutsch orthop Gesellsch **23** 230 1929

muscle and calcaneus with silk thread, but the thread was left with no tension at all. Here atrophy occurred until the gastrocnemius had nearly disappeared. No histologic study was made of these muscles. This bears out the observations of Meyer<sup>28</sup> that atrophy occurs in relaxed muscles.

The amount of shortening of the muscle and of individual fibers in the series of rat muscles is shown by the following figures. The total length of the normal muscles averaged 30.4 mm. and of the shortened muscles, 26.3 mm., which is a shortening of 13 per cent. The minimum shortening was six per cent, the maximum 22 per cent. The individual fibers measured in the normal gastrocnemius averaged 101 mm. in length, and in the shortened ones, 68 mm. This was a decrease of 32 per cent in length. These figures are similar to those found for tetanus muscle. The oblique course of the fibers through the muscle would account in part for the discrepancy between the amount which the whole muscle was shortened and that which the individual fibers shortened.

*Microscopic Changes*—After tenotomy as in tetanus contracture, the greatest alteration occurred in the arrangement and the staining properties of the myofibrils. Longitudinal striation was more pronounced and cross-striation blurred. The blurring of the cross-striation came about in different ways, for the histologic picture was not a uniform one, since adjacent fibers in a specimen frequently had quite different appearances. This is well illustrated in figure 2. Some fibers or portions of fibers were thrown into a wavy contour and the fibrils therefore twisted so that when cut in longitudinal section, one could see cut ends of fibrils alternating with regions of distorted cross-striations running obliquely across the fiber in one direction or another according to the direction of the fibrils at that place (fig. 2, *d* and *e*). Under low power magnification these fibers were striped across with light and dark. This, however, is quite different from the light and dark mottled staining found in other fibers and illustrated in figure 2, fiber *a*, and figures 3 and 4. The mottled staining referred to here is similar to that seen in tetanus contracture. It seemed to be due in part to a loss of affinity for stain in some portions of a fiber, while adjacent areas in the same fiber stained normally or darker than normal, showing a gradation into the nonstaining or lightly staining areas. The configuration of these areas was very irregular, sometimes taking the form of fairly wide zigzag bands across the fiber, sometimes interlacing to give a lattice-like effect as seen in figure 3. The lattice-like appearance was intensified by the separation of the fibrils which produced

28 Meyer, A. W. Theorie der Muskelatrophie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **35** 651, 1922.

the longitudinal fibrillation. Figure 4 which is a higher magnification of fibers *a*, *b* and *c* of figure 3 shows this very well. In a number of fibers regions were seen in which the same group of isotropic and anisotropic bands could readily be traced across normally or darkly staining and lightly or nonstaining areas. In some regions they maintained their normal spacings; in others the *I* band was narrowed. As was the case in tetanus contracture, no definite relation could be seen between the dark and light staining regions of the fiber and the regions in which the stripes were normal or narrowed. Both narrowed and normal spacings were found in both light and dark regions as can be seen in figure 4. The mottling could not therefore be attributed to contraction of the fiber in spots. The possibility that this effect might be due to poor differentiation was eliminated by checking the iron hematoxylin sections with others stained by picrotuchsin, hematoxylin and eosin and Mallory's triple stain, all of which showed mottling of the same regions. Neither could fixation be responsible, since mottling occurred after all of the three fixatives used. In tetanus there were in addition to normally staining and lightly staining areas in fibers regions that stained very darkly and in which the striations were obscured except at the edges where a dark field joined a light one. Here also one occasionally found lightly stained stretched areas between the very dark ones. Such extreme contrasts were not seen in the contracture from tenotomy.

Besides mottled fibers there were others that stained very lightly throughout with cross-striations barely visible. Still other fibers illustrated in figure 2 *b* and *c* had blurred cross-striations resulting from a loss of alignment of myofibrils so that the *I* bands and the *Q* bands in adjacent fibrils did not lie in line and the striations did not therefore appear continuous all the way across the fiber as is the case in the normal fibers shown in figure 1. The loss of alignment seemed to be due to rupture of the interfibrillar portions of those membranes (*Z* membranes) that bind the myofibrils together. Small groups of fibrils or individual fibrils became separated from their fellows and were displaced slightly in a longitudinal direction breaking up the continuity of cross-striation.

In some muscles all of the aforementioned changes could be found side by side. Other muscles showed only one or two of the changes. Six of the seventeen animals studied failed to show mottled fibers. This included the three that had regained function through growth of connective tissue between the cut ends of their tendons. The presence or absence of mottled staining was not dependent on the degree of shortening, however, for two rat muscles showing it very well had shortened 19 and 13 per cent, while another that had shortened 22 per cent had none at all. The three rats which had had their tendons cut



Fig 1—Longitudinal section of normal gastrocnemius (rat) Iron hematoxylin,  $\times 395$

Fig 2—Longitudinal section of gastrocnemius (rat) sixteen days after section of tendo achillis (a) blurred striations, mottled staining, (b) and (c) loss of alignment in myofibrils, (d) and (e) wavy fibers Iron hematoxylin,  $\times 395$

Fig 3—Longitudinal section of gastrocnemius (cat 1) seventeen days after section of tendo achillis, showing mottled staining, longitudinal fibrillation Iron hematoxylin,  $\times 110$

Fig 4—Higher magnification of figure 3, fibers a b and c,  $\times 395$  a and c show lattice effect in staining, (b), very small fiber, thought to be a red fiber squeezed between two pale fibers

for forty-two days had muscles that were 6, 13 and 19 per cent shorter than the normal and none of them had mottled fibers.

The thickening of the fibers resulting from their shortening was apparent in longitudinal as well as in transverse sections. The difference in size of the fibers of normal muscle and muscle in contracture is illustrated by figures 5 and 6. Figure 5 is from the gastrocnemius in contracture and figure 6 from the normal gastrocnemius of rat 8. The areas photographed were taken from approximately the same regions of the two gastrocnemii. The muscles in contracture always stained more lightly and looked less dense than the normal ones. In both longitudinal and transverse sections the myofibrils seemed not to be packed so close together as in normal muscle. This coupled with a decreased affinity of parts of the fibrils themselves for the stain would account for the lighter histologic picture.

Clearly defined vacuoles were present in scattered fibers in only half of the animals studied. Vacuolation here differed from that seen in tetanus in number and distribution of vacuoles. Here they usually occurred singly as seen in cross-section and rarely were nuclei seen near a vacuole within the fiber, whereas in tetanus several vacuoles with nuclei at their edges were often seen in one fiber.

Degenerative changes such as were seen in tetanus did not appear in these experiments. There were no fibers in which the contractile substance had been replaced by nuclei and none in which it had degenerated to a homogeneous mass. Nuclei deeply situated within the fibers were seen in both normal and contracted muscle, in some cases in greater numbers on the side of contracture, in others more on the normal side. Since the gastrocnemius is a mixed muscle the red fibers could account for the appearance of nuclei in this position. In a very few fibers observed in the shortened muscle a small group of fragmented or shrunken nuclei was seen deeply situated. These nuclei may have invaded the fibers from outside or they may have been degenerating muscle nuclei for they stained more darkly than normal muscle nuclei. This, however, occurred in a very small number of fibers and was even seen once in normal muscle, so it seems to have little significance.

There was not a marked increase in muscle nuclei. Some specimens showed no increase, others showed a slight increase with loss of orderly arrangement where the fibrils were twisted. Occasional groups of two or three large rounded nuclei overlapping one another were found in both shortened and normal muscle but more frequently on the side of contracture. In some instances these appeared to be situated in the fiber, but since the same type of rounded, lightly staining nuclei were also seen outside of fibers and frequently associated with capillaries running across fibers, but readily distinguishable from endothelial nuclei, it is thought that they may have been the nuclei of connective tissue wandering cells. Distortion of the fibers may have caused these



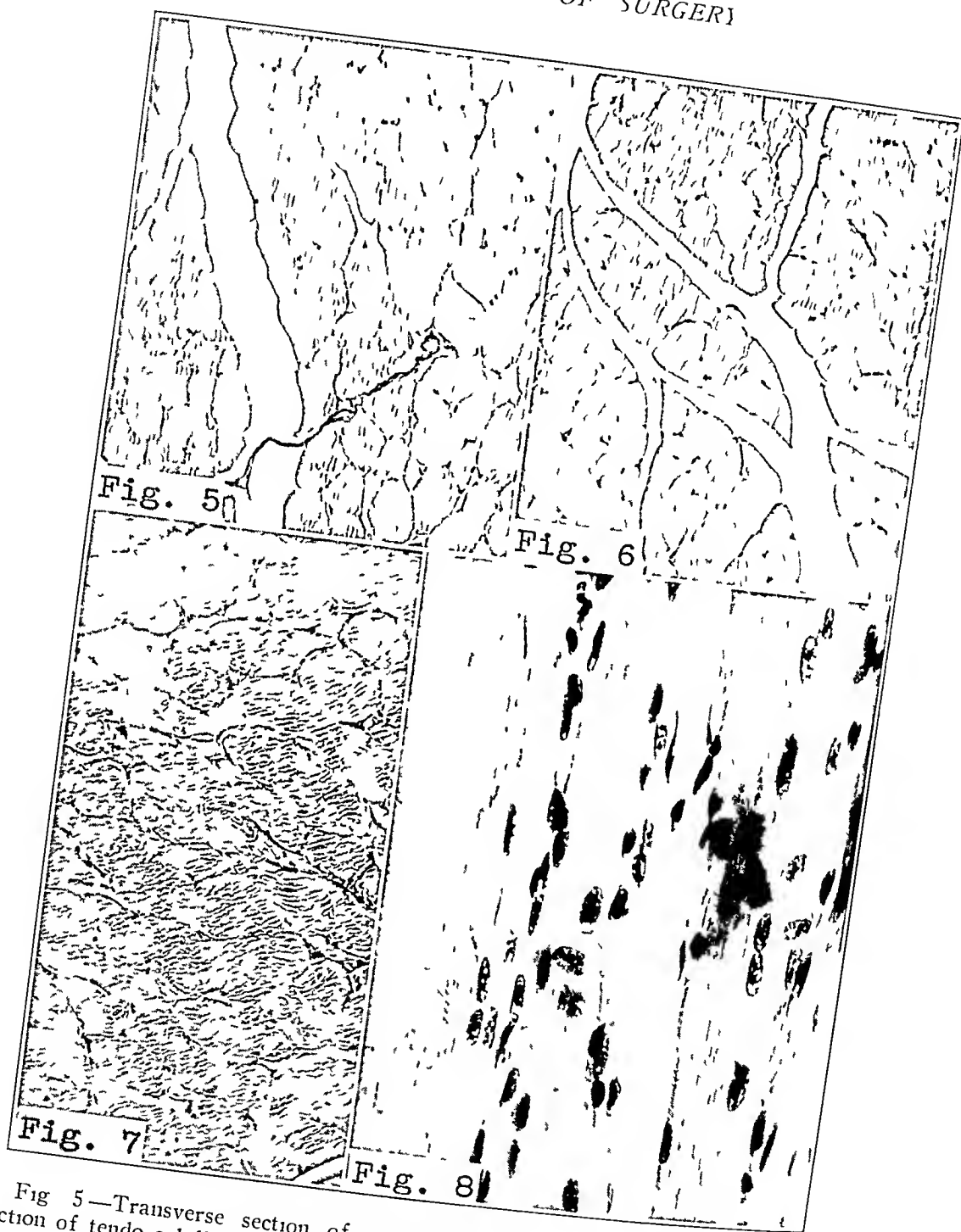


Fig 5—Transverse section of gastrocnemius of rat 8 sixteen days after section of tendo achillis Van Gieson stain,  $\times 110$

Fig 6—Transverse section of normal gastrocnemius of rat 8, taken from the reg on corresponding to that shown in figure 5 Van Gieson stain,  $\times 110$

Fig 7—Transverse section of gastrocnemius of cat 2, seventeen days after section of tendo achillis, showing flattened and more darkly stained red fibers between the larger more rounded pale fibers Van Gieson stain,  $\times 110$

Fig 8—Longitudinal section of gastrocnemius of cat 1 showing type of nuclei in vicinity of blood vessel, that were increased in numbers in the shortened muscles Hematoxylin and eosin,  $\times 450$

nuclei to appear as though they were embedded in the fibers. Three of this type of nuclei are illustrated in figure 8. Two of them appear below the branched capillary in the center of the field and one above it. Of the two below the capillary, the lowermost one focuses in a higher plane than the one nearest the capillary. A third elongated nucleus not in focus and just to the left of the two mentioned is more deeply situated and seems to be a muscle nucleus. Endothelial nuclei are seen in both the upper and lower branches of the capillary. In two of the cats there was an increase in the typical elongated muscle nuclei and an increase in the nuclei of connective tissue wandering cell type in the region of capillaries. Most of the rats showed only an increase in this latter type of nuclei without any discernible difference in number of muscle nuclei. A few short chains containing from three to eleven muscle nuclei were present in both normal and contracted muscle. They were no more numerous in the contracted muscle than in the normal, and therefore cannot be considered characteristic of contracture or essentially pathologic as they are in myotonia atrophica, where there are many chains and the nuclei in individual chains may number forty or more (Heidenham,<sup>29</sup> Weil and Keschner,<sup>30</sup>)

An increase in connective tissue between fascicles or between fibers was difficult to determine by differential staining with van Gieson's picrofuchsin, or with Mallory's triple stain. Comparison of cross-sectional areas from the same parts of contracted and control muscles in rats showed no more connective tissue on the side of contracture than on the normal (figures 5 and 6). The connective tissue in the specimens of cat and guinea-pig muscle differed in appearance on the two sides. In the shortened muscle it stained deep pink with acid fuchsin, while in the normal it was red. The thin bands of connective tissue separating the fibers of the shortened muscle seemed a little broader and less dense than the normal, in which they formed a very sharp outline for the fibers. It seems possible that a change may have taken place in the character of the connective tissue without an actual increase in quantity. Another observation that would point to either an increase in quantity or in tensile strength in the connective tissue was the difference between the behavior of the shortened muscle and the normal during the processes of preparation for staining. When frozen sections were made for fat staining both longitudinal and cross-sections of the muscles in contracture held together throughout the process of staining and mounting whereas the normal ones tore apart very easily and the separation occurred between the fibers. In paraffin embedded blocks taken from

29 Heidenham, M. Ueber progressive Veränderungen der Muskulatur bei Myotonia atrophica, Beitr. z. path. Anat. u. z. allg. Path. **64** 198, 1918.

30 Weil, A. and Keschner, M. Ein Beitrag zur Klinik und Pathologie der Dystrophia myotonica, Ztschr. f. d. ges. Neurol. u. Psychiat. **108** 687, 1927.

the same gastrocnemii as the blocks for frozen sections, shortened muscles cut more easily and did not have a tendency to shatter like the normal ones. Both shortened and control muscles received exactly the same treatment throughout fixation, embedding and staining.

The difference in cutting of the paraffin sections might also be due to changes in the muscle fibers which would prevent the shortened muscles from hardening so much in dehydration and embedding as the normal ones. A comparison of the relative amounts of water in shortened and normal muscles was not made in this series of experiments. Lipschutz and Audova<sup>31</sup> and Audova<sup>32</sup> found that the relative amount of water in the rabbit's gastrocnemius was greater after the achilles tendon had been cut or after nerve section than in normal muscle.

The atrophy which was indicated by loss of weight was not apparent microscopically unless the lighter staining centers of some fibers near the tendon be considered early atrophy though they have been seen in tetanus muscle where there was no loss of weight. Buzzard and Greenfield<sup>32</sup> illustrate similar fibers in early degeneration of muscles in amyotrophic lateral sclerosis, contrasting them with advanced atrophy in the same disease where many fibers have shrunk in size and others have been replaced by fibrous connective tissue. Froboese<sup>33</sup> found that gastrocnemius muscle undergoing atrophy as a result of being inactivated for from three to five weeks in the relaxed state by plaster bandages, showed an increase in nuclei, in connective tissue, and, in high grade cases (four to five weeks in plaster cast) a typical fatty degeneration with definite disappearance of muscle fibers. Since his preparations were in plaster bandages, there may have been interference with circulation which produced some of the alteration. The duration of his experiments was also longer than ours. In our preparations there was only a slight increase in the number of muscle nuclei in some of the animals, no apparent difference in others and no increase in connective tissue. Since the fibrils in the shortened muscles were not so tightly packed together as normal and the Cohnheim's areas more prominent it seems possible that there might have been a thinning out of the fibrillar substance in all of the fibers.

The cats and guinea-pigs showed a somewhat different picture from the rats, of both normal and shortened muscle, in that there was a greater difference in the size of fibers in the same specimen. There were numerous small fibers scattered among the larger ones throughout the cross-sections. In the shortened muscle these small fibers retained

31 Lipschutz, A., and Audova, A. Comparative Atrophy of Skeletal Muscle After Cutting the Nerve and After Cutting the Tendon, *J. Physiol.* **55** 300, 1921.

32 Buzzard, E. F., and Greenfield, J. G. *Pathology of the Nervous System* London, Constable, 1921, p. 275.

33 Froboese, C. Histologische Befunde zur Theorie der Muskelatrophie, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **35** 683, 1922.

then angular outlines and seemed to be crushed between the larger fibers which had increased in size over the normal and presented a rounded outline. Figure 7 shows the difference in size and shape of the fibers in cat muscle in contracture. As stained with van Gieson's stain, most of the small angular fibers in normal and the small flattened ones in contracted muscle were somewhat darker yellow. Alkaline sudan III as used by Ewald<sup>34</sup> and recommended by Denny-Brown<sup>35</sup> for the study of pale and opaque fibers was used on frozen sections of the same muscles to find out whether the flattened fibers were red fibers. This stain colors granules in the muscle fibers red and the remainder of the muscle substance a very light pinkish orange. The flattened fibers on the side of contracture were rich in red granules and stained darker than the large rounded fibers in the same specimens. Since these flattened fibers stained in the manner characteristic of red fibers with sudan III as well as with the usual stains employed for muscle their identification as such seemed justified. The reason for their failure to swell and maintain a more nearly cylindrical form as the pale ones did in the contracted muscles is not apparent.

No fatty degeneration or increase in fat between the fibers could be demonstrated with fat stains.

Though no series of experiments was carried out with the intention of investigating the possibility of recovery, it was noted that the three rats that were allowed to live forty-four days after tenotomy had recovered function in their legs. Two of them were able to walk quite normally, raising their ankles well off the floor and were able to push back with considerable force against a finger placed behind the toes. The third rat was able to raise the ankle from the floor but not quite so high as the other two and was not able to push back with the toes with as much force as the others. The shortening of the gastrocnemius in the first two was 6 and 13 per cent, while it was 19 per cent in the third. All three had developed new functioning tendons formed by connective tissue filling in the space between the cut ends of the old tendon. A similar growth of connective tissue between the cut ends of the tendo achillis in dogs has been described by Frantz, Stout and Clarke.<sup>36</sup> In these dogs only the skin wound was sutured. Function was partially restored when the connective tissue growth had formed a strong enough bond between the ends of the

34 Ewald W. Ueber helle und trübe Muskelfasern bei Wirbeltieren und beim Menschen, *Abhandl. Senckenberg. Nat. Ges. Frankfurt-on-Main*, **31** 109 1912.

35 Denny-Brown D. The Histological Features of Striped Muscle in Relation to its Functional Activity. *Proc. Roy. Soc. Series B*, **104** 371 1929.

36 Frantz V. K., Stout A. P. and Clarke W. C. *Surgical Pathology*, in Nelson's *Looseleaf Surgery*, New York, Thomas Nelson & Sons, vol. 1, chapter 4 p. 301.

tendon Sections were made to determine the nature of the tissue filling the gap in the tendon, but no microscopic study of the muscle was reported

The histologic picture of the rat's gastrocnemius that was only 6 per cent shorter than its fellow of the opposite side was essentially normal, that of the other two showed only a few of the changes seen in material taken a shorter time after tenotomy As would be expected with 13 per cent and 19 per cent shortening, cross-sections showed that the fibers of the muscle that had been in contracture were larger than those of the unoperated leg There was no mottled staining, no loss of alignment of myofibrils and only a few wavy fibers The chief variation from normal in these muscles was a narrowing of the *I* bands in some of the fibers giving a very fine striation Some fibers in the sections had normal spacings of the bands

Ranson and Ranson<sup>37</sup> carried out a series of experiments to determine the extent to which muscles may recover from tetanus contracture They produced local tetanus by injection of a sublethal dose of tetanus toxin into one hind limb of rats paired by weight and age One of each pair was killed at the height of contracture (seven to thirteen days after injection) and the other allowed to live until function returned (fifty-six to one hundred and ten days) All of those killed at the height of contracture showed the typical picture of tetanus contracture while those in which the function had returned to normal had a normal histologic picture, showing clear cross-striation, no nuclear changes, and no apparent increase in fibrous connective tissue The absence of marked changes in the rats that had regained function following tenotomy, together with the recovery from tetanus just described, appears to give some support to the idea that the changes seen in the muscle after tenotomy are not irreparable and that with reestablishment of continuity in the tendon and a return of function the structure of the muscle may also become normal This, however, requires further investigation

#### COMMENT

A comparison of the contracture caused by tenotomy with that caused by tetanus toxin reveals several changes common to both and a few that are not The size and shape of the shortened muscle was the same in both Increased vascularity characteristic of tetanus muscle in gross aspect was absent in the muscles contracted following tenotomy The amount of shortening in the two contractures was similar In the tenotomy series, the gastrocnemius was completely freed from tension by section of the achilles tendon, so that it was free to draw up without restraint In tetanus contracture, however, the muscle was freed only

<sup>37</sup> Ranson, Stephen and Ranson, S W Recovery from Myostatic Contracture Caused by Tetanus Toxin Arch Path 7 949 (June) 1929

from the tension of antagonistic muscles by section of the patellar tendon. Nevertheless, it pulled against the achilles tendon and became as short and thick as the otherwise normal muscles of the tenotomy series that had been completely freed by section of the achilles tendon.

No atrophy was shown by a loss of weight in tetanus, but after tenotomy there was a 20 per cent loss. In making this comparison it must be remembered that the length of time that elapsed in the two series of experiments was different, for the animals with contracture from tetanus were killed in from five to eight days, while the shortest period after tenotomy was sixteen days. Ranson and Ranson<sup>37</sup> found some atrophy even after recovery from tetanus contracture in fifty-six to one hundred and ten days, but not in the seven to thirteen day period in which their controls were killed.

Mottled staining was common to both contractures but occurred in greater extremes in tetanus, for there the beginning degeneration of the contractile substance added to the contrast in the affinity of the different parts of the fibers for the stains. In tetanus, the homogeneous masses in some of the fibers stained very dark, but contracture following tenotomy produced few regions that stained darker than normal, and none of these were the result of degeneration such as was seen in tetanus.

The variations in ratio between the width of isotropic and anisotropic bands were similar in both contractures. However, stretched areas, where the *I* bands had increased to twice their normal width and adjoining portions of fibers where the *Q* bands had approached so close as to nearly obscure the *I* bands, were present in tetanus contracture and absent in that following tenotomy.

Nuclear aggregations which replaced the contractile substance in portions of the sarcolemma tube were found in tetanus but not after tenotomy. This is not surprising, for the introduction of a toxin or other foreign substance might be expected to cause some degeneration even in a short period. Forbus<sup>38</sup> found similar replacement of contractile substance by nuclei in the rectus abdominis muscles in patients with pneumonia and in degeneration experimentally produced by the injection of phenol, alcohol or boiling water. Wisbaum<sup>39</sup> observed it in the psoas and quadriceps in a fatal case of tetanus complicated by pneumonia. Degeneration of portions of the contractile substance into homogeneous or granular masses was not present after tenotomy.

38 Forbus, W. D. Pathologic Changes in Voluntary Muscle. I. Degeneration and Regeneration of Abdominis Rectus in Pneumonia. *Arch. Path.* **2**: 318 (Sept.) 1926, II. Experimental Study of Degeneration and Regeneration of Striated Muscle with Vital Stains. *ibid.* **2**: 486 (Sept.) 1926.

39 Wisbaum, K. Histopathologische Nerven- und Muskeluntersuchungen eines Tetanusfalles, *Deutsche Ztschr. f. Nervenheilk.* **80**: 75, 1923.

Connective tissue was not demonstrably increased in either contracture, though nuclei of the wandering cell type were more plentiful in both

Both contractures had a slight increase in number of muscle nuclei in scattered fibers, but it was not marked in either. In tetanus and after tenotomy, the nuclei in some but not in all specimens appeared a little swollen and stained a little less intensely than normal with hematoxylin.

No difference in the shape of red fibers was observed in rats in either tetanus contracture or in that after tenotomy. Since neither cats nor guinea-pigs were used in the study of tetanus it is not known whether the inability of the red fibers to retain their cylindrical forms against the swelling of the pale fibers is characteristic of contracture or peculiar to contracture after tenotomy in these animals.

None of the changes described account for the inability of these muscles to relax from the shortened state; that is to say, it is not evident why the loss of regular transverse striation should be associated with a shortening of the muscle fibers.

#### SUMMARY

Myostatic contractures produced in two different ways (by tetanus toxin and by tenotomy) have the following histologic alterations in common: (1) increase in diameter of fibers, (2) more pronounced longitudinal fibrillation, (3) blurred cross-striations, (4) dissociation of membranes holding myofibrils in alignment, (5) wavy contour in some of the fibers, (6) light and dark irregularly outlined bands across some of the fibers, due, in part, to loss of affinity for stains in parts of the fibers, (7) increase in nuclei of wandering cell type, (8) slight increase in muscle nuclei in scattered fibers, (9) no increase in connective tissue that can be demonstrated histologically, and (10) a very irregular histologic picture with the various changes occurring side by side in the same or adjacent fibers.

Myostatic contracture due to tenotomy differs from that caused by tetanus toxin in the following ways:

1. The increased vascularity of tetanus muscle is not present in the contracture due to tenotomy.

2. There is a 20 per cent loss of weight in the gastrocnemius after tenotomy, but no atrophy in tetanus in the period required to produce contracture, i. e., from five to eight days.

3. Degenerative changes consisting of disintegration of contractile substance in some fibers and replacement of contractile substance by aggregations of nuclei within the sarcolemma in others are present in tetanus contracture but not in that due to tenotomy.

# PERIOSTEAL LIPOMA

## REPORT OF TWO CASES<sup>\*</sup>

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Malignant tumors arising from the periosteum or from structures immediately adjacent to the periosteum and growing out away from the bone without erosion of the bone cortex or invasion of the medullary cavity have been described by Ewing<sup>1</sup> and Codman.<sup>2</sup> At present these tumors are included among the bone tumors in the classification adopted by the Sarcoma Committee of the American College of Surgeons under the heading of periosteal fibrosarcoma. Since the publication of the classification of the Bone Sarcoma Committee much discussion has arisen as to whether these tumors rightly belong with bone tumors because they seem to have no tendency to involve the bone and because there is no proof that they arise from bone structures.

My purpose in this article is to report two cases of benign tumor which seem to bear the same relationship to bone in that they seem to have developed from the outer layers of the periosteum or the structures immediately adjacent to the periosteum.

## REPORT OF CASES

CASE 1—M. S., a white boy, aged 7, was admitted to the University of California Hospital on July 10, 1919, with a history of tumor of the left arm of about five years' duration that had gradually increased in size. He first came under observation about twenty days before admission to the hospital because of a supracondylar fracture of the opposite or right humerus. The tumor was located on the front of the arm just above the elbow. There was no complaint of pain, tenderness, redness of the skin, etc., no limitation of motion in the elbow joint, no swelling of the limb below the elbow and no anesthetics or atrophies below the elbow.

Examination showed a rather firm elastic tumor on the ventral aspect of the left arm just above the elbow. The mass measured 10 by 12 cm. in its greatest and narrowest diameters. The overlying skin was normal but seemed to be firmly adherent to the growth. Lateral mobility of the tumor was moderately free but movement in the longitudinal axis of the limb was practically nil. Roentgenograms (figs. 1 and 2) showed an apparently encapsulated growth lying immediately

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Submitted for publication, April 2, 1930.

<sup>\*</sup> From the Department of Surgery, University of California.

<sup>1</sup> Ewing, James. Review of Classification of Bone Sarcoma. *Arch. Surg.* 4: 485 (May) 1922.

<sup>2</sup> Codman, E. A. *Bone Sarcoma*. New York: Paul B. Hoeber, 1925, p. 5.



against the bone but not eroding it or causing pressure atrophy. There was a question of slight change in shape, that is, a hollowing out of the ventral surface of the humerus. The tumor did not seem to be lobulated, but showed fanlike, radiating markings in the anteroposterior view. This phenomenon was lacking in the lateral view, which showed rather a mottling and an indefinite trabeculation.



Fig 1—Lipoma lying against the anterior surface of the humerus. Note the smooth outline, the slight mottling and the saddle-like relationship with the humerus, also the lack of erosion of bone and of thinning of cortex.

Under a tentative clinical diagnosis of ganglion or bursa, the tumor was explored on July 11, 1919. The skin was split over the tumor in the longitudinal axis of the limb. It was necessary to split the biceps muscle in order to get at the tumor, which lay immediately beneath this muscle and against the bone. It overlapped on both sides of the bone and came level with or slightly dorsal to

the posterior surface of the humerus. There was a definite, tough capsule, and the tumor shelled out readily on all sides except where it came in contact with the ventral surface of the bone. Here it was adherent for a distance of from 6 to 8 cm up to the shaft from the elbow joint over an area from 2 to 3 cm wide. Sharp dissection was required throughout this area for separation of the tumor

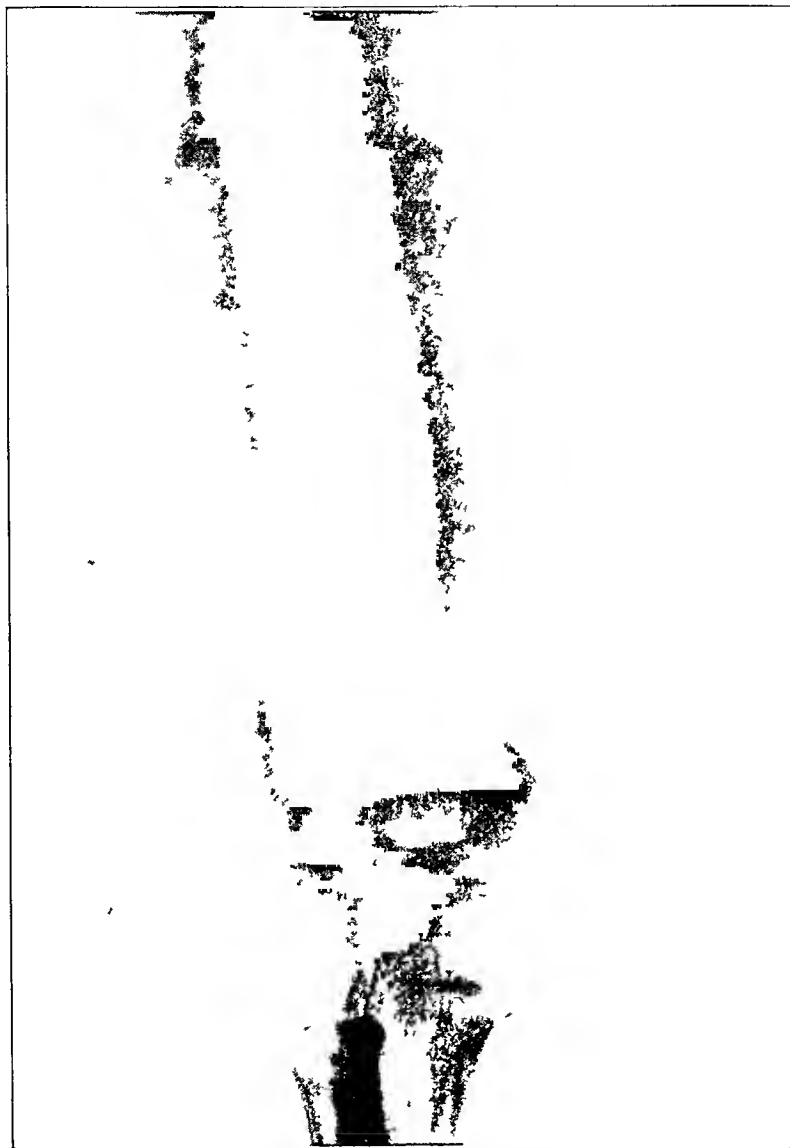


Fig 2—Lipoma of the bone on the anterior surface of the humerus. Note the trabeculation and the fanlike arrangement of the fibrous tissue.

from the bone. After removal of the growth there seemed to be a much thickened periosteum remaining, as if a portion of the tumor capsule had been left behind. Inspection of the mass, however, proved that the capsule was intact at all points, but that the tumor was deeply grooved by the humerus. The wound was closed tight and healing by primary union took place.

The patient was discharged from the hospital seven days after the operation. The ultimate recovery was complete without impairment of the motor or sensory functions and with full motion in the elbow joint. There has been no recurrence.

The pathologic report described a sharply encapsulated, slightly lobulated tumor the cut surface of which was yellowish white, suggesting a large fat content. Microscopic sections showed typical adult, fatty tissue interspersed with rather frequent heavy strands of connective tissue. The final diagnosis was fibrolipoma.

CASE 2—F. S., a white boy, aged 6, was admitted to the University of California Hospital on April 11, 1927, with a history of gradual, uniform enlargement of the leg below the right knee for three years with rapid development of a definite mass during the last five or six months. No pain, tenderness, redness or discoloration of the skin, no limping and no impairment of the patient's general health were noted. There was no history of illness, except the usual children's diseases and occasional colds. The height, weight and mentality were normal.

The left leg showed a general bulging just below the knee, and a tumor mass could be felt estimated to be about 18 by 10 cm. in size and apparently lying in the midst of the muscle of the calf. There was no redness of the skin but the subcutaneous veins were moderately dilated over the tumor, and there was some dilatation of the veins as high up as the groin. The tumor was of firm consistency, not fluctuant and not bony hard. It could be demonstrated as lying posterior to the tibia and fibula and largely to the tibial side. The patient could move all of the joints of this limb, including those of the toes. There were no swellings of the leg or foot and no sensory changes. All laboratory tests gave normal results, including tests of the urine and stool, complete blood tests and Wassermann examinations of the blood. Roentgenograms (figs. 3, 4 and 5) showed a sharply limited and apparently encapsulated mass lying firmly against the posterior surface of the tibia and causing considerable bowing forward of that bone, together with pressure atrophy of a small area in the cortex of the fibula. There were typical trabeculations and suggestive lobulations. There was no evidence of erosion or thinning of the cortex of the tibia. The epiphyses of both leg bones were normal.

Under a clinical diagnosis of fibrolipoma, the tumor was explored on April 15, 1927. It was found to be a firm, well encapsulated, lobulated tumor lying between the gastrocnemius muscles and the bones. The tumor could be reached best by lateral retraction of the gastrocnemius muscles. It shelled out fairly easily, except where it came in contact with the posterior surface of the tibia. Here it had to be peeled off of the bone, mostly by sharp dissection. After removal of the tumor, the periosteum of the tibia was still intact and seemingly considerably thickened, suggesting that a part of the capsule of the tumor had been left behind, although inspection of the tumor showed that the capsule everywhere was intact. Bleeding was negligible, and the wound was closed without drainage.

The postoperative course was uneventful, except for some swelling of the leg below the wound and the formation of an hematoma. The latter was drained, and the wound healed completely by the twelfth day. The patient was discharged as well and able to walk on April 30, that is, fourteen days after operation. Subsequently there has been no recurrence.

The gross specimen showed a lobulated, bosselated, encapsulated mass measuring 8 by 9 cm. in greatest and shortest diameters. The cut surface had the yellowish appearance of fat, and on macroscopic examination the impression was that it was a lipoma. Sections showed the adult type of fat cells intermixed with a great many rather heavy sheets of dense fibrous tissue. The final diagnosis was fibrolipoma.

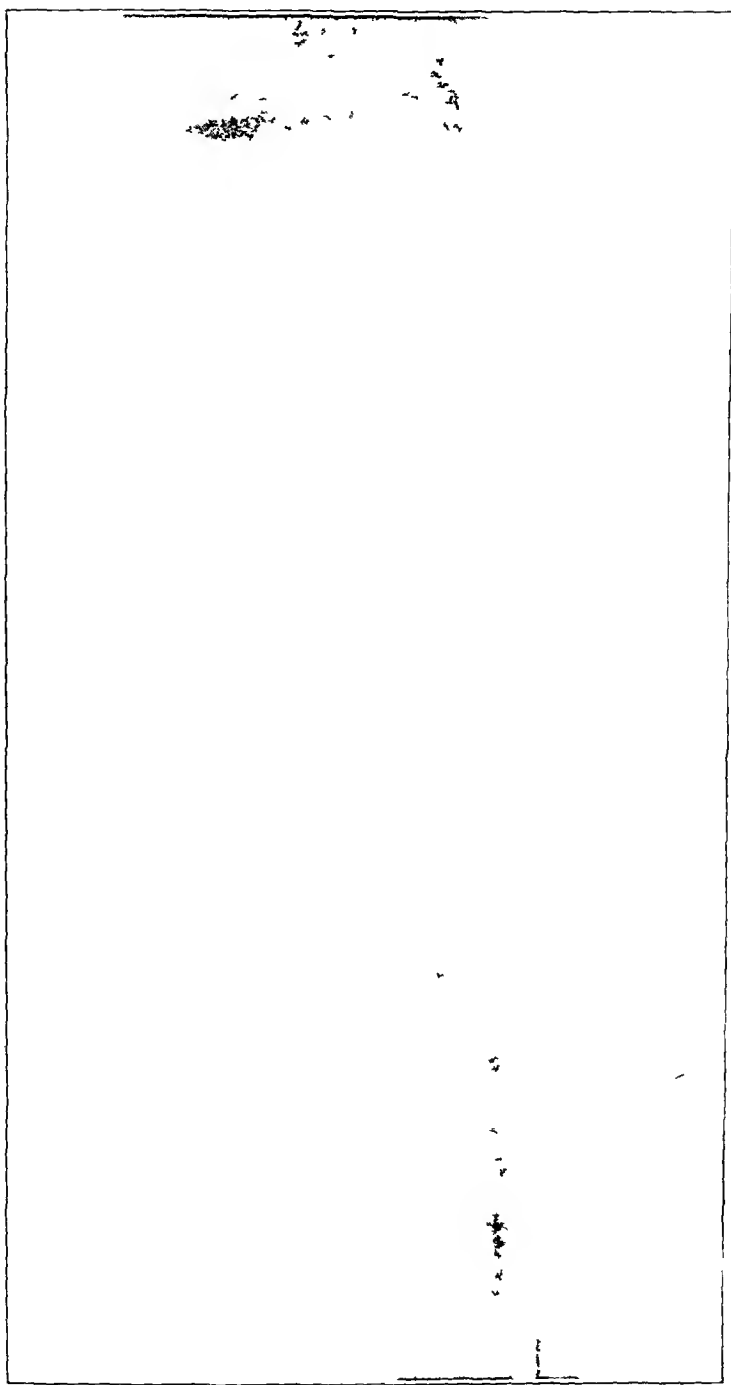


Fig 3—Lipoma lying against the posterior surface of the tibia. Note the mottling and the sharp limits of the tumor.



Fig 4—Lipoma against the posterior surface of the tibia causing marked bowing of the upper end without erosion or thinning of the cortex

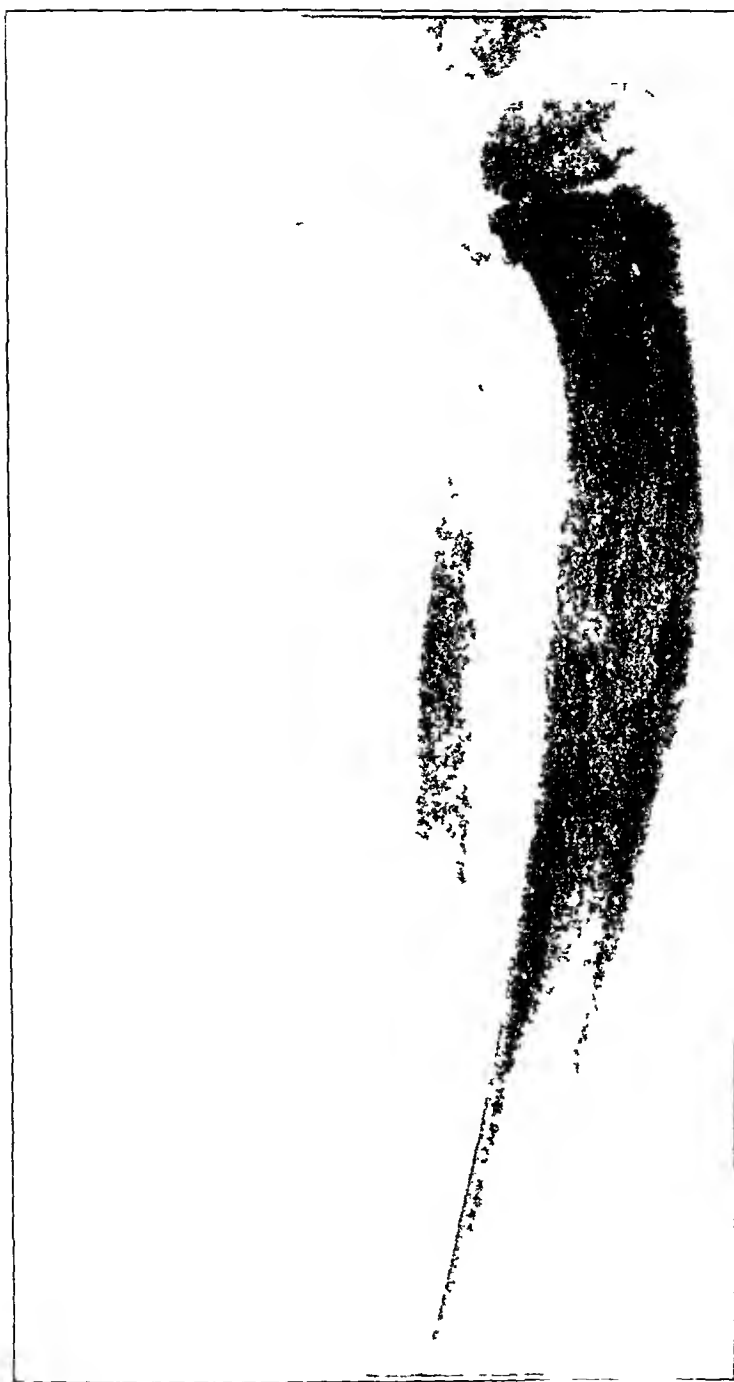


Fig 5—Lipoma of bone against the posterior surface of tibia shown in oblique view. Note the depression on the surface of the fibula. This was erroneously interpreted before operation as atrophy of bone through pressure or erosion. It proved to be a saucer-like depression and the cortex was not thinned.

## COMMENT

The foregoing cases presented some difficulties in making a positive clinical diagnosis. The first tumor was erroneously suspected of being a bursa of some sort, because the x-ray picture was the first one of its type the author had encountered. Malignancy was not considered because of the large size of the growth, the intact periosteum, the very sharp limits of the tumor and the normal condition of the overlying skin and soft parts. At operation the tumor capsule and periosteum merged together so completely that there was no line of cleavage. The tumor had to be separated from the bone by sharp dissection, what seemed to be the outer layers of the thickened periosteum being taken with the tumor. The close blending of the periosteum and tumor capsule is not easily explainable on the basis of contact alone, and there were no fascial planes at this point from which the tumor could originate.

The second tumor was clinically diagnosed lipoma because of the similarity between its x-ray picture and that in the first case. The characteristics in common between the two pictures which pointed to a diagnosis of lipoma were the peculiar form of trabeculation, the very sharp limits and the tendency to alter the shape of the bone by pressure without erosion or bone atrophy. The second case showed what seemed to be an erosion of the fibula, and this caused some doubt regarding the actual benignancy of the growth. The rest of the picture, however, was so overwhelmingly suggestive of benignancy that the area of seeming erosion was disregarded as probably artefact. This was explained at operation, when it was discovered that the flattening of the cortex of the normal fibula caused a shallow, saucer-like depression to resemble erosion when viewed tangentially. Again the tumor capsule had to be separated from the periosteum by sharp dissection, but in this case there were fascial planes from which the tumor might have arisen. Still the total lack of lines of cleavage between the capsule and the periosteum was unexplained.

One would not be justified perhaps in contending that these tumors be called periosteal lipoma or that tumors of this sort should be included under the classification of tumors of the bone. On the other hand, it might not be wholly illogical to look on tumors of this sort as belonging to a group that constitutes the benign counterpart of a malignant group to which the so-called periosteal fibrosarcoma belongs.

# THE EFFECT OF PERICARDIOTOMY ON THE MECHANICS OF THE CIRCULATION \*

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AND

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Since the time when Billroth characterized the operation of tapping the pericardium as "a surgical frivolity and a prostitution of surgical skill," the pericardium has assumed a more important place in surgery. The pericardial cavity has been aspirated for fluid, and it has been incised for pus. It has been opened for the suture of cardiac wounds, for the removal of foreign bodies and for relief from valvular stenoses. The pericardium has been excised when involved by neoplasms. It has been excised, sometimes with the precordial ribs, for adhesive pericarditis and for cardiac hypertrophy. It is apparent that the pericardium has entered the domain of surgery for numerous reasons, and we believe that a fuller appreciation of its pathologic physiology will give it a place of even greater importance than it has held in the past.

Despite the notable progress that has been made along these various lines of endeavor, we have been unable to find, even after an extensive review of the literature, any experimental study of the secondary effects on the mechanics of the circulation brought about by exposing the heart to atmospheric pressure. The only reference that could be found was in an article on experimental pericarditis by Shipley and Horne,<sup>1</sup> in which the following interesting statement appeared: "Because the pressure everywhere within the thorax, except in the lung itself, is lower than atmosphere, one's curiosity is raised as to the effect of atmospheric pressure on the heart after pericardiotomy. Certainly the function of the wall of the chest is to maintain a negative pressure within the thorax and it is not unreasonable to suspect that the heart may be disturbed by exposure to atmospheric pressure."

This paper is based on experiments carried out to determine what effects on the mechanics of the circulation were produced by exposure of the heart to atmospheric pressure.

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\* Submitted for publication, April 7, 1930.

\* From the Laboratory of Surgical Research, the Lakeside Hospital and the Western Reserve University School of Medicine.

\* Read before the Physiological Section of the Federation of American Societies for Experimental Biology, Chicago, March 27, 1930.

<sup>1</sup> Shipley, A. M., and Horne, C. F. Experimental Pericarditis. *Arch. Surg.* 18: 386 (Jan.) 1929.



## METHOD

The determinations that we considered important in a study of this problem were arterial pressure, venous pressure and cardiac output

The method of determining cardiac output was by means of the Fick principle. Before a dog was used for experimentation, he was trained to lie quietly on a table for long periods of time. Male dogs were selected because the pulse rate of the male is more stable than that of the female. After a preliminary period of quiet a rubber mask, devised by Blalock,<sup>2</sup> was placed over the nose and mouth and this was connected to the Benedict spirometer. The oxygen consumption per minute, reduced to standard conditions of temperature and pressure, was determined by taking the average of a six minute curve. Samples of blood were then drawn under oil from the right and left ventricles. The skin and the pleura were usually infiltrated with a few drops of procaine hydrochloride. The oxygen content of 1 cc of these specimens was determined immediately by means of the Van Slyke-Neill<sup>3</sup> manometric apparatus. These specimens were analyzed in duplicate and if the variation in pressure readings exceeded 0.15 mm of mercury, either another set of determinations in duplicate was taken or the specimens were discarded.

According to the Fick formula

$$\frac{\text{Cubic centimeters of O}_2 \text{ consumed per minute}}{\text{Amount of O}_2 \text{ taken up by 1 cc of blood in passing through the lungs}} = \text{Cubic centimeters of blood passing through the lungs per minute}$$

This may be expressed as follows. The oxygen consumption per minute in cubic centimeters divided by the difference in oxygen content of 1 cc of arterial blood and 1 cc of venous blood equals the amount of blood in cubic centimeters put out by the heart per minute.

The foregoing principle and method have been used for much experimental work in the last few years. If the determinations are done under satisfactory conditions, the results will agree with surprising accuracy within a variation of 10 per cent.<sup>4</sup> Occasionally a wide deviation in results is obtained, but this is due either to a mixture of ventricular blood or to the fact that the dog has not maintained his basal level.

The dog does not possess an area on the thoracic wall in contact with the pericardium similar to the "triangle of safety" in the human being, which was described by Voimitch-Sianojentsky.<sup>5</sup> To open the pericardium without opening the chest, it was necessary to suture the pericardium to the thoracic wall as a preliminary step before opening it to atmospheric pressure (figs 1 and 2).

2 Blalock, A. Rubber Mask for Determination of Oxygen Consumption of Dog. *J. Lab. & Clin. Med.* **12** 378 (Jan.) 1927.

3 Van Slyke, Donald D., and Neill, James M. The Determination of Gaseous in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement. *I, J. Biol. Chem.* **61** 523, 1924.

4 Marshall, E. K., Jr. Studies on the Cardiac Output of the Dog. *Am. J. Physiol.* **77** 459 1926.

5 Voimitch-Sianojentsky, A. Die Operationen der Eröffnung des Herzbeutels, und ihre anatomischen Grundlagen. *Arch. f. path. Anat.* **151** 380 1898.

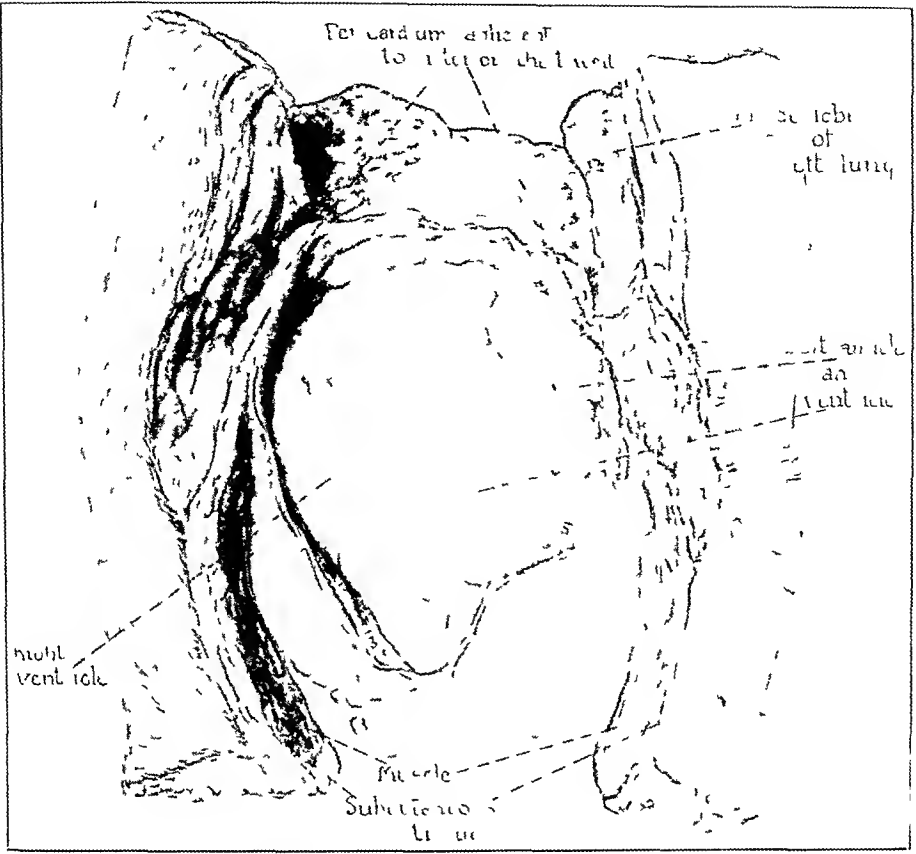


Fig 1—The pericardium had been attached to the thoracic wall and the pericardial cavity opened to the exterior. The drawing shows a portion of the thoracic wall and the pericardium bisected.

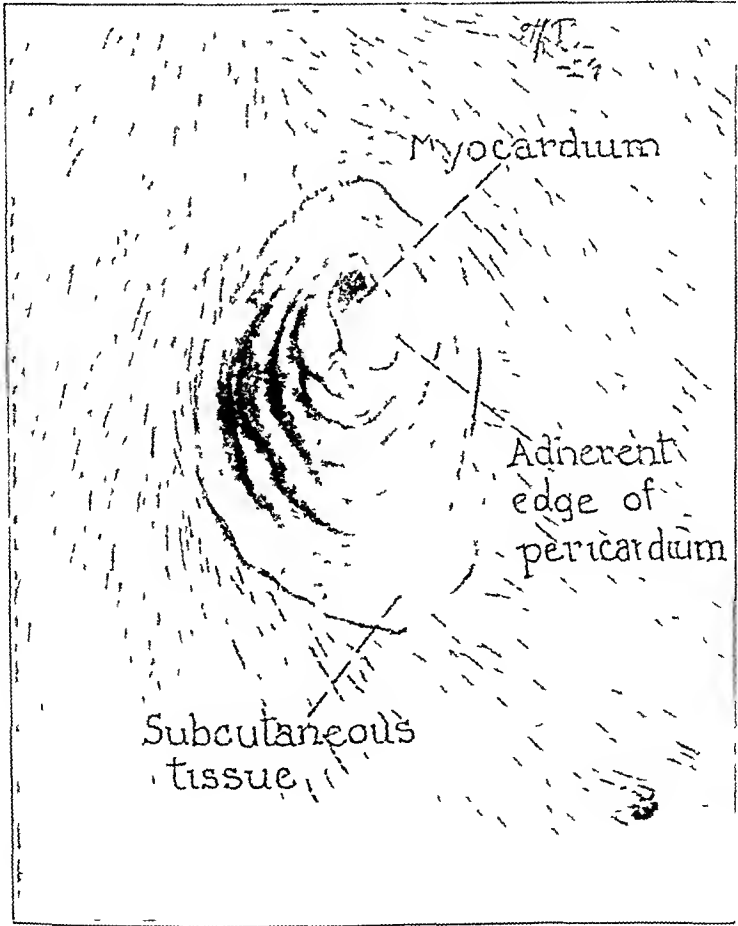


Fig 2—The pericardiostomy as seen from the exterior.

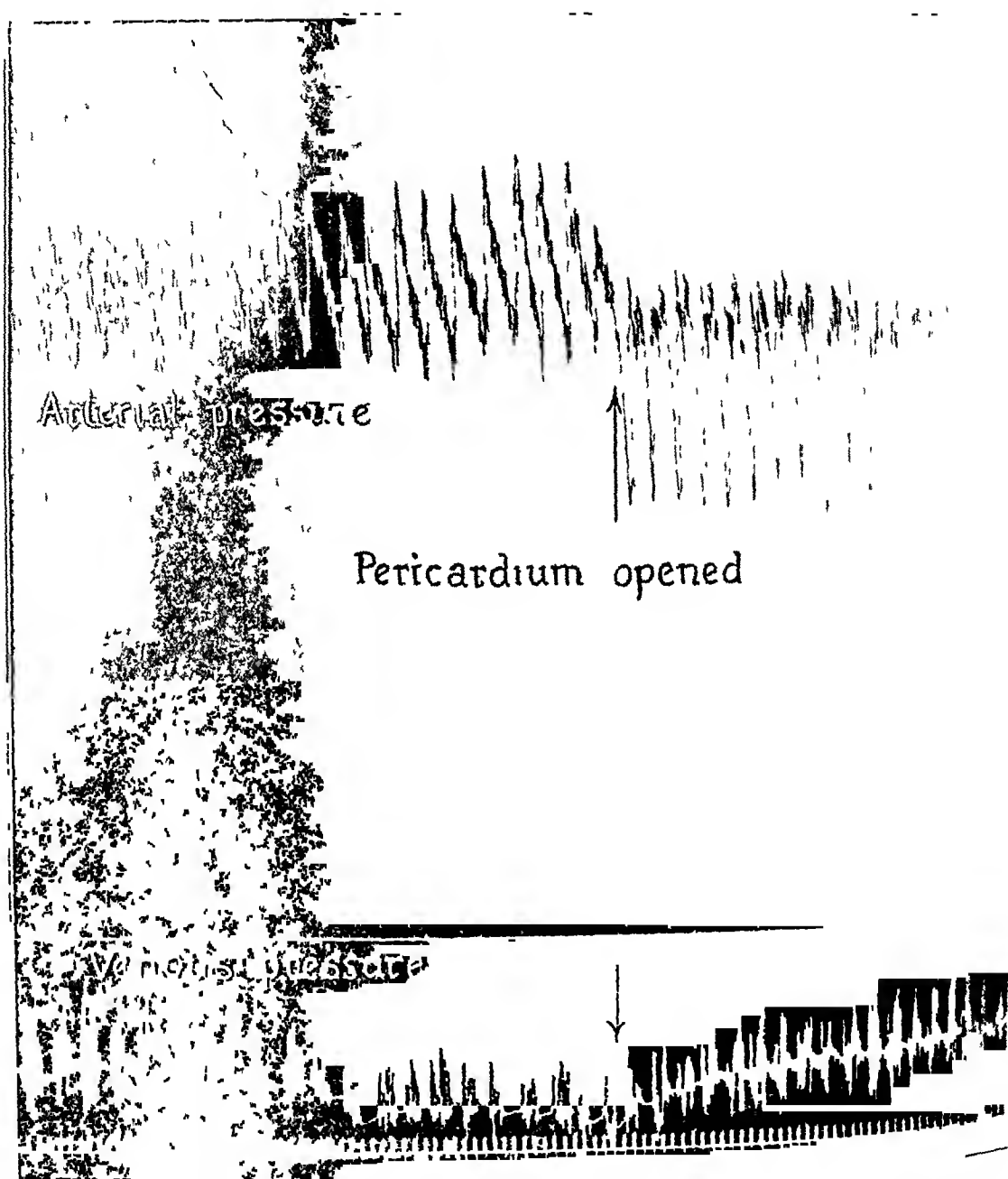
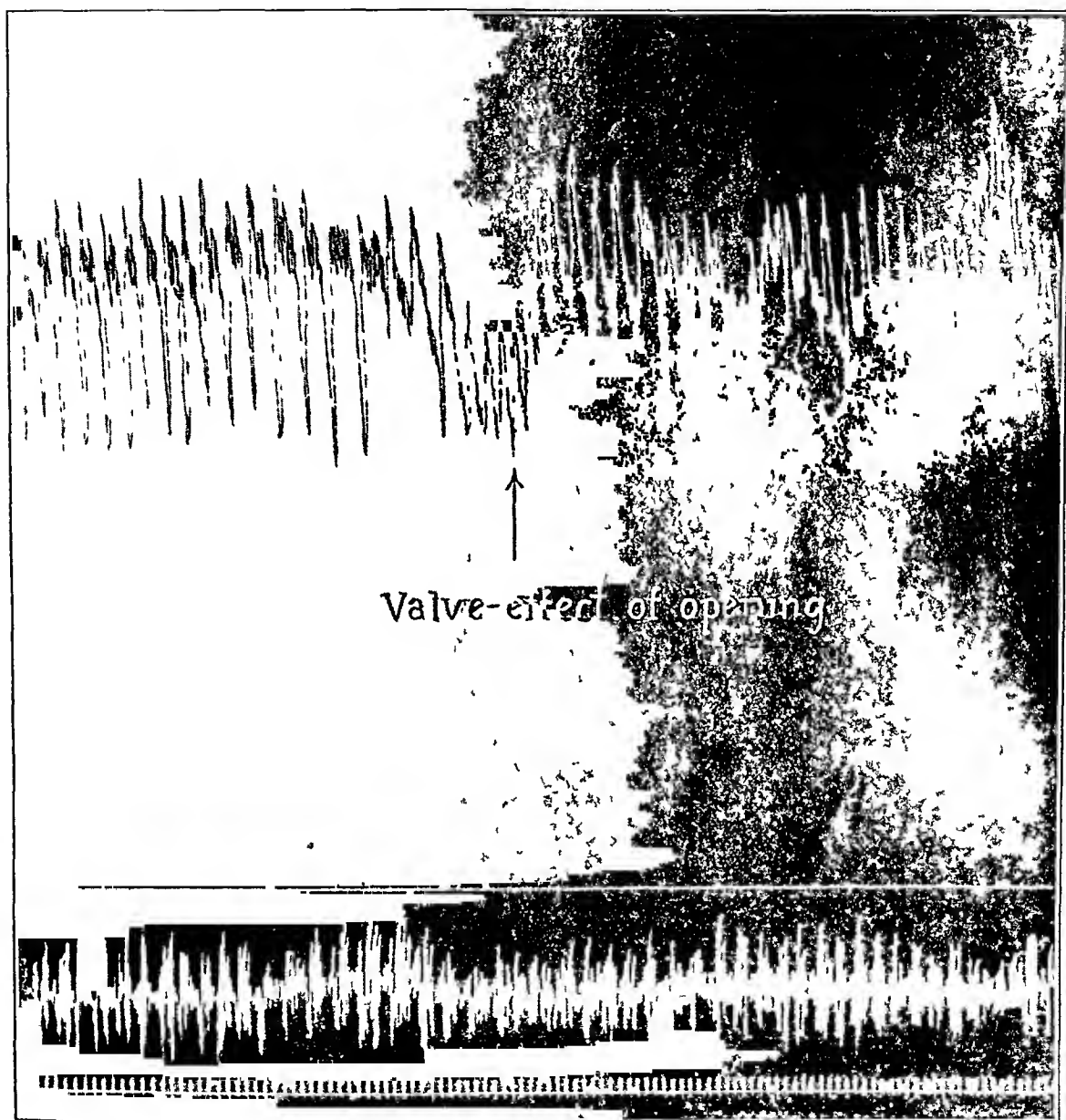


Fig 3—Graph showing the arterial and venous pressures before and after opening the pericardial cavity to the atmosphere. When the pericardial cavity was opened, the arterial



pressure fell from 20 to 30 mm of mercury and the venous pressure rose. The fluctuations in arterial pressure occurred when the opening into the pericardial cavity was partially obstructed.

## BLOOD PRESSURE DETERMINATIONS

EXPERIMENT 1—On Aug 24, 1929, a mongrel bull-dog, weighing 21.6 Kg was anesthetized with ether. Three inches (7.6 cm) of the left fifth rib were resected, and the pericardium was securely sutured to the thoracic wall over an area about 4 cm in diameter. The muscle, subcutaneous tissue and skin were approximated with silk sutures.

On September 19, the dog was in good condition. The wound had healed.

On November 8, 1 Gm of sodium *iso*-amylethylbarbiturate (amytal) was injected intravenously for anesthesia. The left femoral artery was cannulated and connected to a mercury manometer. The left jugular vein was cannulated close to

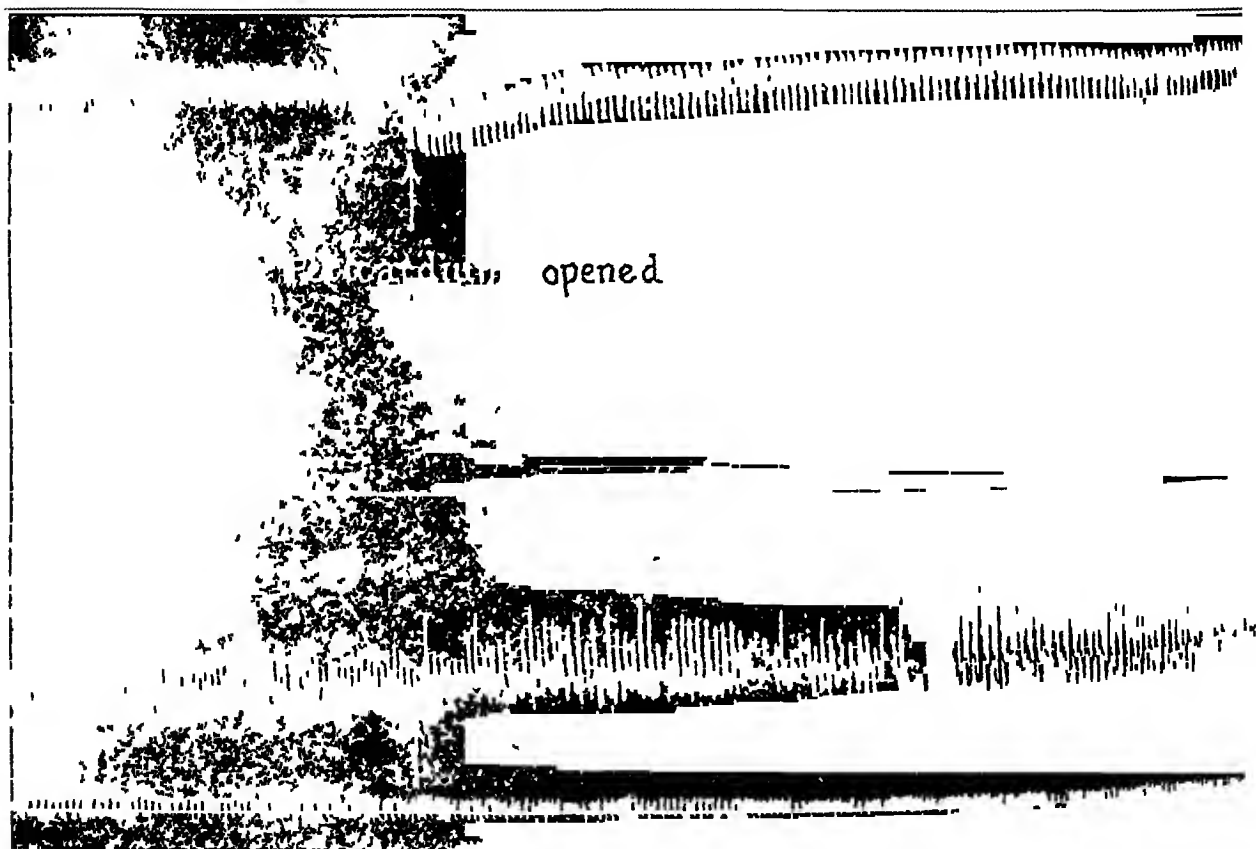


Fig 4—When the pericardial cavity was opened to atmospheric pressure, the arterial pressure fell 10 mm of mercury, and after twenty-eight seconds regained its former level. There was a sustained rise in the venous pressure.

its junction with the innominate and connected to a Marey tambour. Tracings of arterial and venous pressures were obtained.

The scar over the left fifth rib was incised, and the pericardium was opened. When the pericardium was opened, an immediate fall in arterial pressure and a rise in venous pressure took place (fig 3). The fall in arterial pressure measured from 20 to 30 mm of mercury. These pressure changes were sustained. The egress and ingress of air in the pericardial cavity were demonstrable, and when this passage of air was obstructed by placing the soft tissues in the opening of the pericardium the arterial pressure fell still further. Within a few seconds the arterial pressure swung to a higher level and then fell again.

The foregoing experiment was repeated.

EXPERIMENT 2—On June 6, 1929, a dog weighing 21 Kg was anesthetized with ether, and the pericardium was sutured to the thoracic wall

On August 26, under ether anesthesia, a femoral artery and a jugular vein were cannulated, and pressure determinations were taken. The pericardium was then opened to atmospheric pressure. There occurred immediately a slight but definite fall in arterial pressure and a rise in venous pressure.

EXPERIMENT 3—On June 28, 1929, the pericardium was sutured to the thoracic wall, and subsequently the cavity was opened to atmospheric pressure. The dog was utilized for a long series of cardiac output determinations (see succeeding material).

The pericardiostomy wound healed, and the pericardial cavity became sealed from atmospheric pressure. Under ethyl carbamate anesthesia, the left femoral

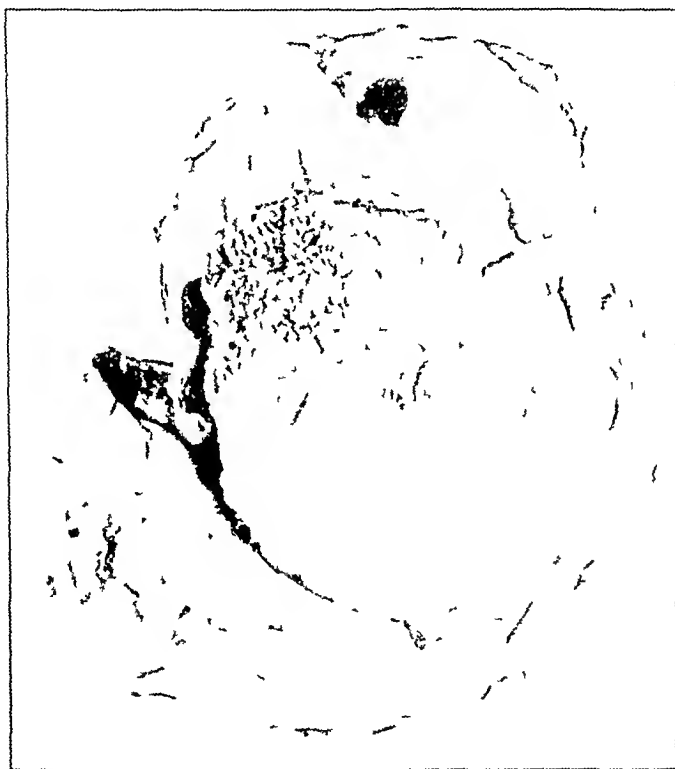


Fig 5—The positive atmospheric pressure within the pericardial cavity and the negative pressure within the pleural space produced some dilatation of the pericardial cavity. The latter is more capacious than normal.

artery and the left jugular vein were cannulated. The former was connected to a mercury manometer and the latter to a Marek tambour. Pressure tracings were taken. The thoracic scar was incised and the pericardial cavity was opened to atmospheric pressure. As soon as air entered the pericardial cavity, the arterial pressure fell and the venous pressure rose (fig 4). The fall in arterial pressure measured about 10 mm of mercury and was transient, the pressure regaining its former level in twenty-eight seconds. The rise in venous pressure was sustained.

At necropsy the pericardial cavity was definitely more capacious than normal. It was increased in its transverse diameter and it extended superiorly over the great vessels at the base of the heart, producing a condition similar to the dilatation that occurs in cases of pericardial effusion (fig 5).

EXPERIMENT 4—On June 7, 1929, the dog weighed 24 Kg. The first stage operation was carried out under ether anesthesia.

On June 28, arterial and venous pressure determinations were made under ethyl carbamate anesthesia. When the pericardium was opened to atmospheric pressure, the arterial pressure fell 20 mm of mercury and the venous pressure slightly but definitely increased. The arterial pressure regained its former level in twenty seconds, the venous pressure remained elevated throughout the experiment. The dog was killed.

#### COMMENT

It is apparent from the preceding experiments that when the pericardial cavity was opened to atmospheric pressure, a fall in arterial pressure and a rise in venous pressure occurred. These pressure changes were always definite. In one experiment the fall in arterial pressure was slight, measuring from 6 to 8 mm of mercury. In another experiment a fall of 10 mm occurred, and this fall in pressure persisted twenty-eight seconds before the former level was regained (fig 4). In another experiment the fall in arterial pressure measured from 20 to 30 mm of mercury, and this pressure change was sustained throughout the experiment (fig 3). When the opening into the pericardial cavity was closed by placing soft tissues into it, fluctuation in pressure occurred. This fluctuation was probably related to changes in intrapericardial pressure brought about by respiration, but these changes did not seem to synchronize with the respiratory cycle. In each experiment the venous pressure showed a definite increase when the pericardium was opened, and the rise was maintained throughout the experiment.

The explanation of these pressure changes is apparent. As the pericardium is a collapsible structure, it readily yields to the intrathoracic pressure changes that accompany inspiration and expiration. The intrapericardial pressure, therefore, may be assumed to be the same as the intrathoracic pressure. These recurring pressure changes (from  $-4.64$  mm at the end of quiet inspiration to  $-3.02$  mm of mercury at the end of expiration<sup>6</sup>) play an important rôle in the filling of the heart. Because of the negative pressure in the thorax, the pressure in the great veins at the base of the heart is very low. According to Burton-Opitz,<sup>7</sup> the pressure in the superior vena cava near the auricle in the dog was  $-2.96$  mm of mercury.

When the pericardium is opened to the atmosphere, the negative intrapericardial pressure is changed to the positive atmospheric pressure. This increased intrapericardial pressure expresses itself in two ways. It has a dilating effect on the pericardium and increases the size of the cavity in a manner similar to that produced by pericardial effusions. It also exerts a compression effect on all intrapericardial structures.

6 Aron, quoted by Howell. *Physiology*. Philadelphia, W. B. Saunders Company, 1915, p. 659.

7 Burton-Opitz, R. Venous Pressures. *Am J Physiol* 9:198, 1903.

including the ventricles, the auricles and the great arteries and veins. Of these structures, the intrapericardial portions of the superior and inferior venae cavae carry the least pressure, and presumably it is on these great veins that the compression effect of atmospheric pressure is relatively the greatest. From a consideration of the usual negative pressure existing within the venae cavae and the portion within the pericardial cavity, one would expect collapse of the great veins. This, however, is undoubtedly prevented by the immediate accumulation of blood in the great veins assembling a transmitted pressure from the periphery. This pressure is sufficient to drive the blood into the heart against the positive atmospheric pressure within the pericardium.

The pressure changes obtained in the foregoing experiments suggest that an increase in the venous pressure is necessary to overcome the positive intrapericardial pressure of the atmosphere. The slight decrease in arterial pressure indicates that this positive atmospheric pressure

TABLE 1—*Cardiac Output Determinations in Experiment 5*

	Oxygen Consumption, Cc per Minute	Oxygen Content, per Cent by Volume, 1 Cc of Blood		Arterial Venous Difference	Cardiac Output,* Cc per Minute	Pulse Rate
		Arterial	Venous			
Before opening pericardium	87.4	20.80	16.93	3.87	2.258	144
After opening pericardium	88.9	21.48	15.85	5.63	1.570	192

\* The fall in the cardiac output was .50 per cent.

constitutes a handicap to the cardiac function. This is brought about chiefly by the impairment to the filling of the heart although the direct pressure increment on the ventricles and auricles may also be a factor. The problem was studied further by cardiac output determinations taken before and after the pericardial cavity was opened to the atmosphere.

#### CARDIAC OUTPUT DETERMINATIONS

EXPERIMENT 5—On Sept. 5, 1929, a male mongrel dog weighing 11 Kg. was anesthetized with ether and the pericardium was sutured to the left thoracic wall as described in preceding experiments.

On October 24, under sodium iso-amylbarbiturate anesthesia the left femoral artery and the left jugular vein were cannulated and attached to a mercury manometer and a Marek tambour, respectively. An oxygen consumption curve and samples of the right and the left ventricular blood were taken before and after the pericardium was opened to atmospheric pressure. The dog was killed by ether narcosis.

Immediately after the pericardial cavity was opened the arterial pressure dropped from 130 to 120 mm. of mercury and the venous pressure showed a slight but definite rise. The arterial pressure regained its former level in a few seconds, but the rise in venous pressure was maintained throughout the experiment.



The marked drop in the cardiac output obtained in experiment 5 made us question the veracity of results obtained from experiments in which the animals were killed. One of the complications met with in experiments similar to the preceding was a pneumothorax due to the leakage of air through puncture wounds in the pericardium made by the aspirating needle.

The following series of experiments in which the animals were allowed to recover were carried out.

EXPERIMENT 6—On a male mongrel collie weighing 16.5 Kg cardiac output determinations were carried out to determine the normal.

On March 30, 1929, under ether anesthesia about 5 cm of the left fourth rib and costal cartilage was removed. The pericardium was sutured to the thoracic wall, and the muscle, subcutaneous tissue and skin were approximated in layers.

TABLE 2—Cardiac Output Determinations in Experiment 6

	Oxygen Consumption, Cc per Minute	Oxygen Content, per Cent by Volume, 1 Cc of Blood		Arterial Venous Difference	Cardiac Output, Cc per Minute	Pulse Rate
		Arterial	Venous			
Jan 16, 1929	108.22	17.89	13.07	4.82	2,245	96
Jan 29, 1929	100.61	16.78	13.03	3.75	2,683	88
March 8, 1929	126.64	19.21	13.87	5.34	2,345	100
March 8, 1929	123.99	20.85	14.62	6.23	1,900	88
March 27, 1929	98.40	19.63	15.75	3.88	2,537	90
March 28, 1929	86.58	19.35	15.34	4.01	2,159	90
On March 30, the pericardium was sutured to the thoracic wall						
April 12, 1929	79.68	19.56	15.76	3.80	2,097	88
April 17, 1929	91.52	19.44	15.76	3.68	2,487	80
April 29, 1929	103.48	21.51	16.92	4.60	2,250	80
On May 15, the pericardial cavity was opened to atmospheric pressure						
May 17, 1929	97.94	16.92	11.91	5.00	1,959	124
May 18, 1929	91.94	15.74	9.43	6.30	1,459	88
May 19, 1929	87.26	13.08	4.67	8.41	1,069	100
May 20, 1929	104.05	15.21	4.82	10.39	1,001	100
May 22, 1929	96.18	23.18	12.03	11.15	863	100

Cardiac output determinations were repeated.

On May 15, the dog was in good condition, weighing 17 Kg. Morphine, 0.16 Gm, was given. The scar over the left fourth rib was infiltrated with procaine hydrochloride, and the pericardium was incised for about 1 cm, producing a free communication with the atmosphere. The conus arteriosus was visible, and specimens of blood from the right and left ventricles could be obtained easily through the pericardiostomy opening. Cardiac output determinations were repeated, but purulent pericarditis developed after a few days, and thus terminated the experiment.

On May 23, the weight of the dog at necropsy was 14.4 Kg. The pericardial cavity contained about 75 cc of creamy pus. The heart seemed to be dilated, and the epicardium was covered with a thick coating of fibrin and pus. The pericardial cavity was definitely more capacious than normal. The pleural cavity was well sealed off and showed no evidence of infection. There was a small adhesion between the left middle lobe of the lung and the scar in the thoracic wall. The lungs and the abdominal organs appeared normal. A few days before death edema of the hind legs developed.

The average of the cardiac output determinations before and after the pericardium was sutured to the thoracic wall is 2,326 and 2,278 cc, respectively. A cardiac output determination carried out two days after the pericardium was opened showed a decrease of 319 cc, or 14 per cent, from the previous determinations. Subsequent determinations showed a progressive decrease in cardiac output, but these determinations are probably of no significance because of the development of purulent pericarditis.

EXPERIMENT 7—On a male collie weighing 15.12 Kg cardiac output determinations were made to determine the normal.

On Feb. 12, 1929, under ether anesthesia, about 4 cm of the left sixth rib and costal cartilage was removed. The pericardium was sutured to the thoracic

TABLE 3—*Cardiac Output Determinations in Experiment 7*

	Oxygen Consumption, Cc per Minute	Oxygen Content, per Cent by Volume, 1 Cc of Blood		Arterial Venous Difference	Cardiac Output, Cc per Minute	Pulse Rate
		Arterial	Venous			
Jan. 27, 1929	116.84	18.12	12.88	5.26	2,221	88
Feb. 2, 1929	127.57	18.04	12.47	5.57	2,290	74
On February 12, the pericardium was sutured to the thoracic wall						
March 4, 1929	72.72	18.05	14.35	3.70	1,965	78
March 6, 1929	121.28	17.75	11.91	5.84	2,077	88
March 19, 1929	104.24	17.92	12.28	5.64	1,848	80
March 21, 1929	109.70	18.72	13.38	5.34	2,054	88
On March 21, the pericardial cavity was opened to atmospheric pressure						
March 21, 1929	104.72	19.30	12.83	6.47	1,619	72
March 22, 1929	91.11	17.38	10.96	6.42	1,419	140
March 24, 1929	119.43	18.77	11.35	7.42	1,610	110

wall over an area about 3 cm in diameter. The muscle, subcutaneous tissue and skin were approximated with silk sutures.

Cardiac output determinations were repeated.

On March 21, the wound had healed and the dog was in good condition. The scar was infiltrated with procaine hydrochloride, and an opening about 2 cm in diameter was made into the pericardial cavity. Cardiac output determinations were carried out. Subsequently, the dog developed pneumothorax due to the leakage of air through the small holes produced by the aspirating needle.

The dog died on March 25. The left pleural cavity was distended with air, and the left lung was completely collapsed. The right lung was not collapsed. The pericardium was firmly adherent to the thoracic wall to which it had been sutured. The pericardial cavity contained a little frothy fluid, and there was evidence of an early pericarditis. The heart was not dilated. The pericardium was slightly thickened, and the pericardial cavity was larger than normal. The abdomen contained a small amount of free fluid.

It is seen from the determinations in table 3 that there was a slight drop in the cardiac output following the attachment of the pericardium to the thoracic wall. The determinations taken after the pericardium

was opened unfortunately were complicated with pneumothorax, which developed from the small leaks in the pericardium produced by the aspirating needle

The first determination made immediately after the pericardium was opened, however, seemed to have been free from this possible source of error. If this was so, there was a decrease in the cardiac output of 18 per cent when the pericardium was opened to atmospheric pressure.

The same unfortunate complications developed in another experiment, in which twenty determinations had been carried out. There were no readings sufficiently accurate after the pericardium was opened to warrant a record of this experiment.

TABLE 4—*Cardiac Output Determinations in Experiment 3*

	Oxygen Consumption, Cc. per Minute	Oxygen Content, per Cent by Volume, 1 Cc. of Blood		Arterial Venous Difference	Cardiac Output, Cc. per Minute	Pulse Rate
		Arterial	Venous			
Feb. 25, 1929	105.81	15.98	10.87	5.11	2,071	68
March 1, 1929	116.72	18.93	12.45	6.48	1,801	68
March 6, 1929	107.84	15.40	10.43	4.97	2,170	80
On March 18, the pericardium was sutured to the thoracic wall						
April 1, 1929	103.14	16.43	11.06	5.37	1,921	50
April 9, 1929	89.07	17.09	12.44	4.65	1,913	60
On June 4, the pericardial cavity was opened to atmospheric pressure						
June 5, 1929	107.79	18.18	11.40	6.78	1,590	72
June 6, 1929	79.14	16.10	11.08	5.02	1,576	92
June 7, 1929 a.m.	85.23	16.98	10.96	6.02	1,415	96
June 7, 1929 p.m.	93.49	16.50	10.35	6.15	1,520	96
June 12, 1929	96.14	14.68	8.54	6.14	1,567	92
The wound had healed and the opening into the pericardial cavity had closed						
June 19, 1929	95.41	14.99	9.95	5.03	1,894	72

The two succeeding experiments are conclusive.

EXPERIMENT 3—Determinations of normal cardiac output were made on a male collie weighing 14 Kg.

On March 18, 1929, under ether anesthesia, about 4 cm. of the left fifth rib was removed, and the pericardium was sutured to the thoracic wall so that an area about 4 cm. in diameter came into contact with the wall. On June 4, the dog was given 0.16 Gm. of morphine, and the scar was infiltrated with procaine hydrochloride. The pericardial cavity was opened to atmospheric pressure. The dog had been in good condition throughout the experiment, and on June 7 cooperated perfectly for cardiac output determinations. On June 19, the wound had healed so that the opening into the pericardial cavity had become completely obliterated. The condition at this time was equivalent to that before the pericardial cavity was opened (June 4). On June 28, under ethyl carbamate anesthesia, the left femoral artery and the jugular vein were cannulated to a mercury manometer and a Marey tambour, respectively. The pericardium was again opened to atmospheric pressure, and the effect on the arterial and the venous pressures was recorded (fig. 4).

The dog was killed and necropsy was carried out. There were no adhesions between the heart and the pericardium. On the epicardium and the parietal pericardium were a number of small plaques of fibrin covered by a smooth glistening surface. The pericardial cavity was increased in size. This dilatation was similar to that produced by pericardial effusions. There was no evidence of infection. The lungs, the pleural cavities and the abdomen were normal. There was no edema and no evidence of an impaired circulation.

It appears from the determinations in table 4 that the cardiac output decreased about from 300 to 400 cc per minute when the pericardial cavity was opened to atmospheric pressure. This represents a decrease

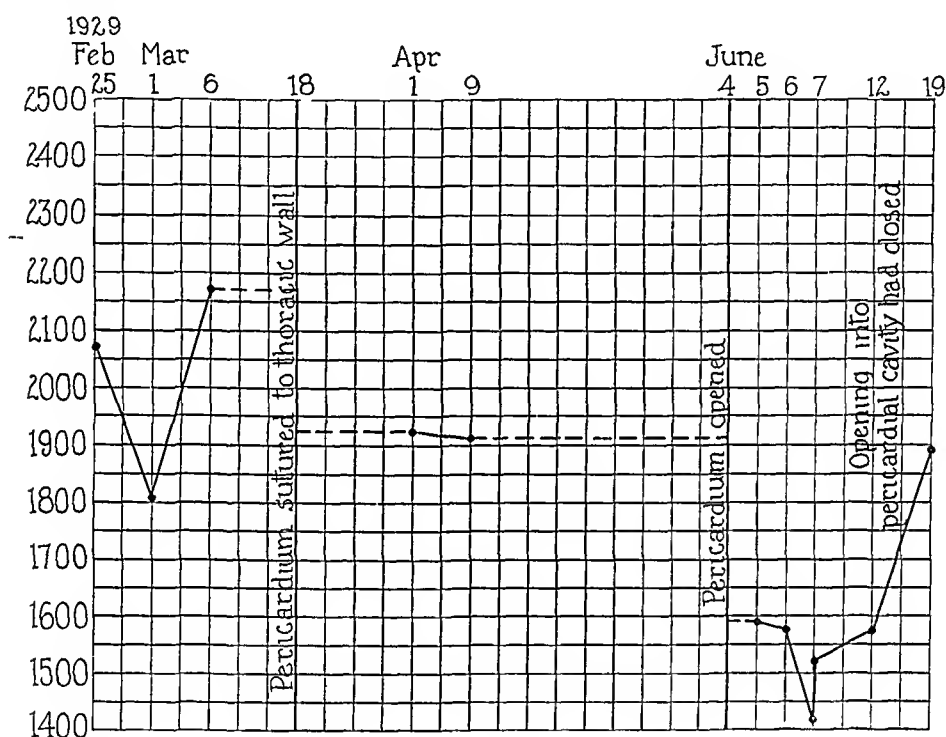


Fig 6—Chart showing the minute volume output of the heart in cubic centimeters before and after the pericardium was sutured to the thoracic wall, after the pericardial cavity was opened to atmospheric pressure and after this opening had closed

of about 20 per cent in the minute output of the heart. It was shown also that after the opening into the pericardial cavity became obliterated by the healing of the wound the cardiac output returned to its former level (fig 6). It also appears from the analyses that the oxygen content of both the left ventricular and the right ventricular blood decreased after the pericardium was opened, and that this decrease was more marked in the mixed venous blood.

**EXPERIMENT 8**—This dog was a female mongrel weighing 150 Kg. On Sept 4, 1929, under ether anesthesia, 3 cm of the left fifth rib was removed, and the pericardium was sutured to the thoracic wall so that an area of the pericardium about 3 cm in diameter came into contact with the thoracic wall.

On December 16, the dog cooperated poorly for cardiac output determination. Many of the determinations are not included because of the great fluctuation from the basal level. Morphine or sodium *iso*-amylethylbarbiturate given intravenously was used as a sedative for some of the studies. The determinations in which drugs were used are so labeled. The cardiac output determinations that were carried out immediately after the pericardial cavity was opened were complicated by pneumothorax. A sufficiently long interval was given for the pneumothorax to disappear, and care was taken subsequently not to pass the aspirating needle through the pericardium in taking samples of blood.

On Jan 2, 1930, a snugly fitting catheter was inserted into the opening of the pericardium and attached to a tambour and writing lever. The egress of air from the pericardial cavity with expiration could be easily felt on the hand. The graph records the passage of air synchronous with respirations (fig 7). When attached to a water manometer having a bore of 4 mm, the fluctuations in the column of water averaged 8 cm.

On January 21, the wound had healed so that the opening into the pericardial cavity had become closed.



Fig 7—Graph indicating the passage of air through the opening into the pericardial cavity.

TABLE 5—Cardiac Output Determinations in Experiment 8

	Oxygen Consumption, Cc per Minute	Oxygen Content, per Cent by Volume, 1 Cc of Blood		Arterial Venous Difference	Cardiac Output, Cc per Minute	Pulse Rate	
		Arterial	Venous				
Sept 20, 1929	97.24	16.65	12.54	4.11	2,366	98	A* 0.5 Gm
Oct 1, 1929	78.94	17.97	14.72	3.25	2,429	140	A 0.5 Gm
Oct 10, 1929	127.85	18.52	12.49	6.03	2,120	116	A 0.5 Gm
Nov 15, 1929	122.96	19.90	14.63	5.28	2,329	92	No drugs
Dec 7, 1929	108.46	20.14	14.39	5.76	1,883	80	M† 0.16 Gm
Dec 16, 1929	79.78	19.67	16.39	3.28	2,432	96	A 0.5 Gm
The pericardial cavity was opened to atmospheric pressure							
Dec 28, 1929	116.19	21.04	13.59	7.45	1,560	144	No drugs
Dec 31, 1929	100.36	19.51	13.96	5.55	1,808	150	No drug
Jan 2, 1930	73.88	15.77	13.30	4.47	1,633	132	A 0.6 Gm
On January 21, the wound had healed and the opening into the pericardial cavity had closed							
Jan 21, 1930	95.87	15.93	12.15	4.79	2,001	126	A 0.5 Gm
Jan 24, 1930	83.77	17.79	14.05	3.74	2,240	112	No drug
Jan 25, 1930	60.18	17.47	13.25	4.22	2,137	92	No drug

\* A indicates sodium *iso*-amylethylbarbiturate anesthesia.

† M indicates morphia anesthesia.

On January 25, the experiment was finished. The dog was in good condition and was not killed.

From the determinations in table 5 it seems that although there were some wide fluctuations, the minute output of the heart fell about 20 per cent when the pericardial cavity was opened to atmospheric pressure. This loss in minute volume output was almost entirely regained after the pericardial cavity became closed from atmospheric pressure (fig. 8).

#### SUMMARY OF DATA

From the experiments it may be concluded that when the pericardial cavity was opened to atmospheric pressure, there occurred 1. A definite

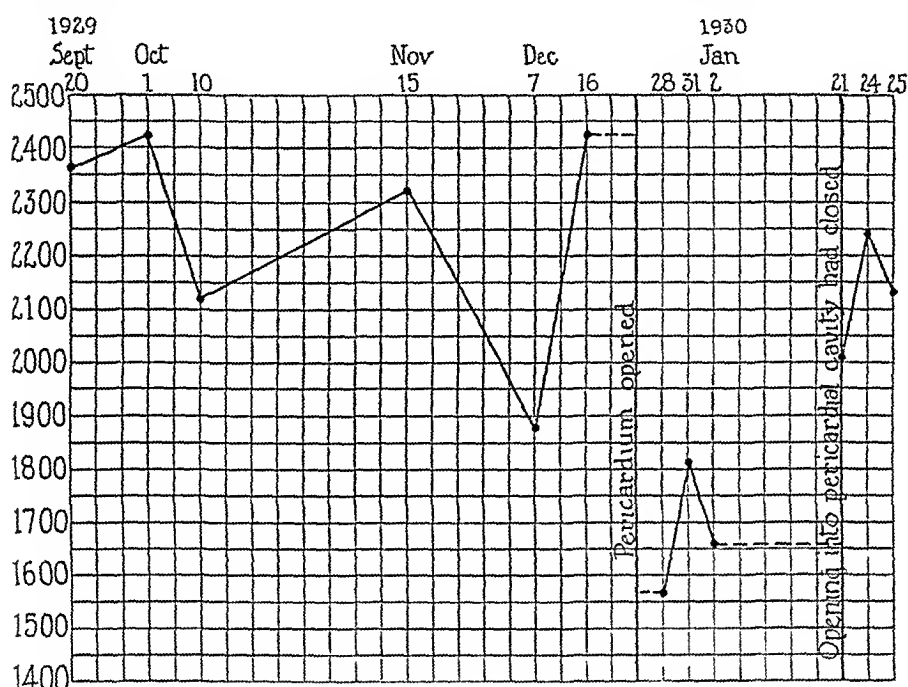


Fig. 8—Chart showing the minute volume output of the heart in cubic centimeters before and after opening the pericardial cavity to atmospheric pressure and after the opening in the pericardial cavity closed.

sustained rise in venous pressure. 2. A fall of from 8 to 30 mm of mercury in the arterial pressure. This decrease in pressure was sustained in one experiment, in others it was transient. 3. A decrease of from 15 to 30 per cent in the minute volume output of the heart. There was a return to almost normal minute volume output following closure of the pericardial opening.

The mechanism producing these changes is a pressure phenomenon. Atmospheric pressure acts as an air tamponade on the heart and the great vessels within the pericardial cavity. It also produces dilatation of the pericardial cavity similar to that produced by the effusion of fluid.

We should like to name this mechanism pneumocardiac tamponade.

## CLINICAL APPLICATION OF THIS MECHANISM

This mechanism may play an important rôle in all cardiac and pericardial surgery. The disturbance to the circulation brought about by exposing or opening the pericardial cavity has been observed by surgeons, but the possible effect of atmospheric pressure has never been considered a factor in the development of cardiac failure occurring at operation when these structures were exposed. Its deleterious effect may well be a vital factor in the cases in which the circulation

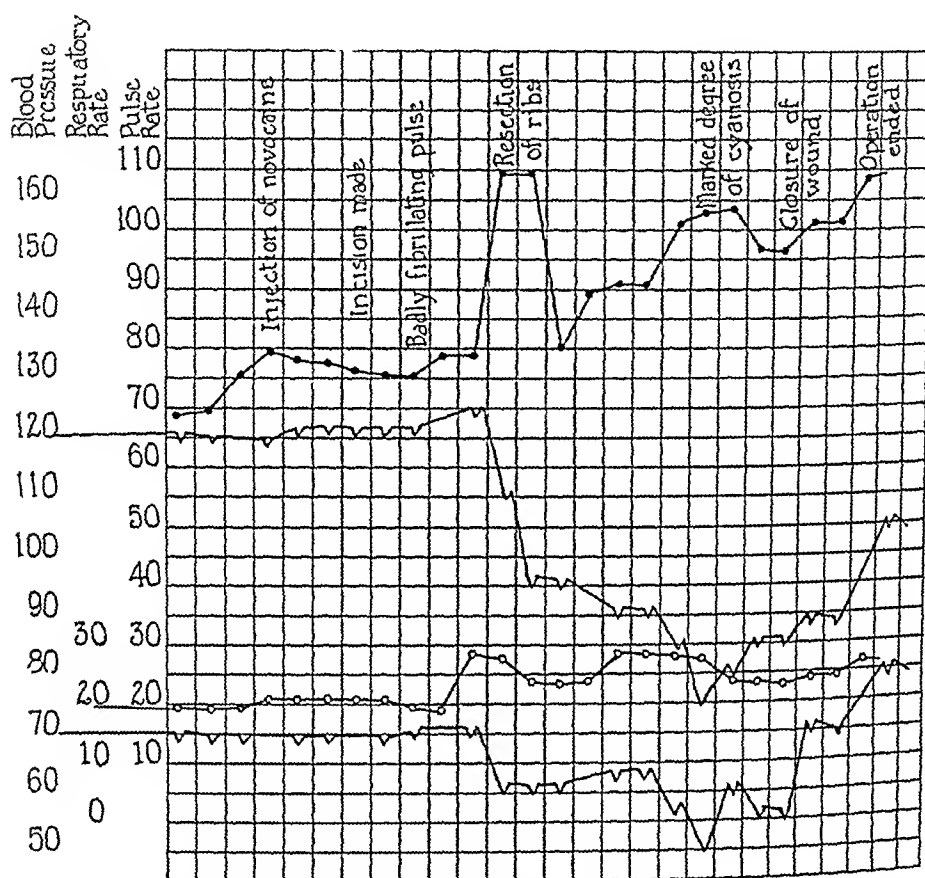


Fig 9—Chart of the pulse rate, blood pressure and respiration taken during the resection of the precordial ribs under local anesthesia in a patient with serious decompensation

is just adequate to maintain life. In such cases, this additional handicap placed on the heart might prove fatal. Such a case is recorded briefly below.

A white man, aged 25, entered the Lakeside Hospital with the complaint of pain over the precordium. At the age of 7 he had had chorea, at 14 he had noted dyspnea, at 20 he had been subjected to sharp stabbing pains localized beneath the left clavicle. For several years he had been an invalid suffering from heart disease, confined to his home and later, to bed.

When admitted to the hospital, the patient appeared to be in a serious condition. He was dyspneic when recumbent, the finger tips and the lips were

cyanotic, and the patient was undernourished. The heart was fibrillating, the rate at the wrist was 70 per minute. The systolic blood pressure was 120 and the diastolic 65. There was an anterior bulge of the precordium. A marked precordial impulse was present. A prolonged systolic murmur and a presystolic thrill and murmur were recorded over the apex. The heart was greatly enlarged, and under the fluoroscope it seemed to be fixed in position. Râles were heard at the base of each lung. Some enlargement of the liver and slight edema of the ankles were present.

The diagnosis of rheumatic heart disease with mitral stenosis and insufficiency was made. The presence of adhesive pericarditis was suspected. For relief from such adhesions and also as a decompression for the enlarged heart, the Brauer operation of cardiolysis was carried out on Sept. 14, 1929.

Under procaine hydrochloride anesthesia, 5 inches (12.7 cm.) of the fourth rib and about 6 inches (15.24 cm.) of the fifth and sixth ribs on the left were removed by subperiosteal resection. The pericardium was incised for the purpose of exploration, but no adhesions were found. The patient withstood the procedure poorly. The blood pressure fell, the pulse rate increased, and the cyanosis became more pronounced. The chart kept by the anesthetist (fig. 9) shows the fall in blood pressure, the decrease in pulse pressure and the rapid pulse rate. It is seen that the fall in pressure occurred approximately at the time when the bony framework was being removed and the pericardium exposed. After the operation was complete, the blood pressure remained low, the pulse rate rapid and the cyanosis extreme. Death occurred twelve hours later.

The tamponade effect produced by atmospheric pressure may be exerted in various types of operation. These include operations on the heart and pericardium and also certain operations on the anterior thoracic wall and mediastinum. It should be noted that the atmospheric pressure can be transmitted on the heart without opening the pericardium. In the selection of cases for operation, the heart should possess a certain reserve power capable of withstanding this tamponade effect.



# A REVIEW OF UROLOGIC SURGERY

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(Concluded from p 866)

## URETHRA

*Ruptures*—Higgins<sup>25</sup> stated that there are three types of rupture of the urethra rupture of the pendulous urethra, rupture of the bulbous urethra and rupture of the intrapelvic urethra. The most common type of rupture is that of the bulbous urethra. The symptoms occurring immediately after this type of rupture usually are pain, hemorrhage from the meatus, difficulty or inability to urinate, tenderness and tumefaction. Perineal hematoma may be present. The degree of trauma is not always indicated by the severity of the symptoms. Although inability to void may be due to a reflex spasm of the compressor urethralis muscle as the result of injury and clots may pass from a minor injury, the history of trauma, of hemorrhage from the meatus and of perineal hematoma associated with inability to void generally indicate rupture of the urethra. Catheterization under strictly aseptic conditions should be attempted. The treatment for incomplete rupture of the urethra still remains a controversial subject. Higgins is satisfied if a soft rubber catheter can be passed into the bladder and believes that perineal section, which has been recommended, should be avoided if possible. If infection supervenes or a catheter cannot be passed into the bladder, perineal section is necessary.

In cases of intrapelvic rupture, the urethra is torn in association with crushing injuries of the pelvis. The rupture usually occurs at the apex of the prostate gland, tearing it from the membranous urethra.

<sup>25</sup> Higgins, C C Rupture of the Urethra, Report of 12 Cases, Surg Gynec Obst 50 639 (March) 1930

The differential diagnosis of this condition and rupture of the bladder may be difficult. If the bladder is distended and palpable, the rupture is below the vesical sphincter. Suprapubic cystotomy and drainage of the space of Retzius should be done as soon as possible. Perineal section is performed from forty-eight to seventy-two hours after preliminary cystotomy. The catheter is passed in a retrograde direction from the bladder to the perineum and then out through the meatus. This catheter acts as a splint holding the neck of the bladder in normal position until the cut ends of the urethra unite. The catheter is usually removed in from forty-eight to seventy-two hours. Instrumentation may safely be instituted from ten to sixteen days after operation. Further treatment should be based on urethroscopic study.

The mortality in cases of rupture of the urethra is low if treatment is given immediately. Stricture may result but under judicious care will respond to treatment.

#### TESTES

*Tumors*—Barringer, Stewart and Spies<sup>26</sup> stated that the formerly grave prognosis in cases of tumor of the testes has materially improved with the advent of irradiation. With adequate irradiation certain types of highly malignant neoplasms may be completely controlled even though demonstrable retroperitoneal metastasis is present. The reaction of tumors of the testis and of the resulting metastatic growth to irradiation is known to be variable. In certain cases the primary tumors and the metastasis disappear precipitately and do not recur within a period of years. In other cases the primary tumors react with varying promptness and usually do not recur, whereas the metastatic growths react well and may completely disappear so far as palpation can show, but recur after an interval. Others are resistant to radiotherapy.

One hundred and fifty cases of neoplasms of the testis are reported, in the majority of which the primary tumor had been removed elsewhere and the patient was referred for treatment by irradiation. In certain instances the primary tumor was never removed, the diagnosis resting on the conformation of the tumor, the presence of palpable metastatic growths and the reaction to irradiation. In 42 of the 150 cases the testis was removed either before or after irradiation and the pathologic examination was made. If irradiation failed to control the tumors, analysis showed that the treatment had not been sufficient and the dosage was practically doubled in such cases. When metastatic growths are enormous and the patient is in general poor health sufficient treatment to control the tumors cannot be given.

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<sup>26</sup> Barringer B. S., Stewart F. W. and Spies J. W. Testicular Neoplasms. *Ann. Surg.* 91: 115, 1930.

The advisability of removing primary tumors of the testis after irradiation is a controversial question. Baringer, Stewart and Spies perform orchidectomy as a routine (1) in order to determine the type of tumor and to gain information as to the probable prognosis and the probable amount of irradiation necessary, (2) to obviate the necessity of subsequent overirradiation of the opposite testis, and (3) to prevent local recurrence in what may be an adult teratoma on the presumption that resumption of activity of more anaplastic portions may recur.

Of 113 patients who received treatment and were traced, 41 are living and clinically free from disease. Of the 113, the condition of 13 was primarily operable without palpable metastasis. Ten (79 per cent) are alive and clinically free from disease. The condition of 16 patients was primarily inoperable with demonstrable metastasis, 4 (25 per cent) are clinically well. Three patients in the operable group had recurrence, they (100 per cent) are all clinically well. Eighty-one patients had recurrent cases with inoperable local recurrences and inoperable metastatic lesions, 24 (30 per cent) are without evidence of disease.

[*Editorial Note*—The variability in radiosensitivity of testicular neoplasms is well emphasized. The fact that sixteen patients with inoperable cases and three with recurrent cases were treated with 25 per cent clinical cure by radiotherapy argues well for this form of treatment if subsequent reports show these results to be consistent.]

A few years ago, Hinman advised extensive radical resection of the regional lymphatic glands as a means of combating tumor of the testis. Young reported 50 per cent of one year cures in eight cases, and rather discouraged irradiation except as a postoperative measure. Probably, as the situation stands, orchidectomy and irradiation will usually give the best results.]

#### EPIDIDYMITIS

*Tuberculosis*—Cecil<sup>27</sup> described an operation for tuberculosis of the epididymis, the object of which is the clean removal of the epididymis and sinuses and the securing of primary healing. The tuberculous sinuses are painted with pure carbolic acid, after the scrotum has been cleansed. An elliptical incision is then made through the skin around the sinus. While the pressure above the testis is still maintained with the hand, light elliptical cuts are made concentrically, dividing bands of tissue directly down to the tunica vaginalis. These concentric cuts are kept close around the elliptical incision in the skin. As the cuts are made, the testis and epididymis begin to extrude from the scrotum. The scrotum is immediately wrapped with warm salt

<sup>27</sup> Cecil, A. B. An Operation for Tuberculosis of the Epididymis, *Surg Gynec Obst* 50 624 (March) 1930.

packs, covered with a towel and kept surgically clean. The tunica vaginalis is opened and the epididymis is separated from the testis. The epididymis and testis are both wrapped in warm salt packs and set aside. A clamp is pushed up along the vas deferens until it corresponds with the external ring. A small nick is made over the tip of this clamp and another clamp, which is used for clamping off the vas, is pushed down along the same path. The vas is cut between two clamps. The clamp and vas are then drawn upward to bring the vas out in the groin, but at no time is the clamp removed from the vas or is the vas ligated, as such attempts are likely to infect the wound. A single stitch is passed through the nick. This stitch passes through the outmost covering of the vas. The clamp, with the vas still fastened in it, is wrapped in gauze and strapped to the abdomen. The scrotum is pulled down over the testis and closed by interrupted dermal sutures. The wound is covered with collodion. The scrotum is supported with a binder. In about seven or eight days the vas comes away at the level of the skin.

#### URINARY LITHIASIS

*Etiology*—Hinman, Charnock and Dart<sup>28</sup> considered some of the hypotheses concerning the etiology of urinary lithiasis which have been subjected to experimental study. Such etiologic agents are diet, mechanical or anatomic features, foreign bodies, infection or micro-organisms and urinary colloids.

The problem of the formation of calculi in which the urinary solids are precipitated as fused, hard concretions rather than individual crystals is one of chemical precipitation. The basis of future knowledge of this problem seems to be in the field of colloidal chemistry. The process which can alter the action of the urinary colloids appears at this time to make up the foundation in the formation of urinary calculi.

In order to check the relation between the hydrogen ion concentration of the urine and the balance of the urinary colloids, a series of experiments was carried out to test the variation of crystalloid precipitation under different hydrogen ion concentrations of the urine. The factors of foreign body and infection were eliminated and stones formed within the pelvis of experimental animals by oxamide. The oxamide is precipitated from the urine in such a way that the individual crystals tend to fuse. It was found that the urine of these rabbits were normally about  $p_H$  7. Three classifications were made, alkaline and normal and the animals were put on a diet which would keep the urine at a relatively

<sup>28</sup> Hinman, F., Charnock, D., and Dart, A. E. Studies of the Etiology of Urinary Lithiasis, Proc. Ninth Meeting Clin. Soc. Genito-Urin. Surg., San Francisco, July, 1929.

wide variation of hydrogen ion concentration. The following points were noted: negative results without signs of concretions or oxamide deposits, fine sand visible macroscopically at necropsy and small concretions of sufficient size to cause urinary stasis when passed into the ureter. It was concluded that in rabbits having a strongly alkaline urine there is a tendency to the formation of stone.

[*Editorial Note*—Keyser, in 1922, studied oxamide lithiasis in rabbits. The reaction of the urine of the rabbits, grossly controlled, seemed to affect little the deposition of oxamide in the urinary tract. Therefore, this report is somewhat in conflict.]

Two points should be made. 1. Oxamide is a crystalloid foreign to the urinary tract of the animal. Therefore, conclusions drawn from a study of the formation of oxamide stones should not be applied directly as pertinent to the usual type of lithiasis seen in animal life. In other words, oxamide lithiasis is not a biologic process, but an unusual manifestation of chemical poisoning. However, the physical features of oxamide lithiasis, such as the fusing of the crystals, does seem to demonstrate the usual process in the formation of urinary calculi, as seen clinically. 2. From clinical evidence it seems fairly certain that the reaction of the urine does have some part in the formation of calculus. The calculi found in the lower animals, such as sheep and dogs, are almost consistently of the carbon variety and are associated with alkaline urine. In human beings phosphate calculi are most frequently associated with alkaline urine and with urea-splitting organisms of the proteus group. Oxalic and uric acid calculi are more often associated with urine of lower hydrogen ion concentration but the ranges have not been accurately determined. Crowell has been able to stop the formation of cystine calculi in a patient by keeping the urine at a range of high alkalinity.

These features would tend to show that the reaction of the urine is of importance in the formation of stone, but in just what physico-chemical manner this factor acts has not as yet been determined.]

*Calculi in Infancy*—Campbell,<sup>29</sup> in reviewing a series of 30 cases of urinary calculi in infancy and childhood, observed that stones of later childhood are usually of urate or calcium phosphatic composition, from 10 to 15 per cent are composed of uric acid. Urinary calculi may appear at any age, they have been found in a 6 and in an 8 month old fetus. Urinary lithiasis is predominantly a disease occurring in boys in a series of 2,000 cases reviewed, only 77 were girls. The ratio of incidence was 17 on the right side to 7 on the left. In about 10 per

<sup>29</sup> Campbell, M. F. Urinary Calculi in Infancy and Childhood. I. A. M. A. 94:1753 (May 31) 1930.

cent the involvement was bilateral. Clinical observations show that the greatest obstacle to the passage of stones occurs at the vesical outlet, undoubtedly an explanation of the higher incidence in the male.

The symptoms of stone are chiefly those of infection of the urinary tract, although pain, whether due to urinary obstruction or to the presence of the foreign body, may be the first symptom apparent to the patient. Pyuria, urinary frequency and dysuria, together with localized, radiating or indistinct pain, are the most constant complaints. Stone without pyuria is rare. The amount of pus varies. A few scattered white blood cells to each high power field and thick, milky urine containing from 30 to 40 per cent of gross pus on standing may be noted. When the stone is renal or ureteral, the radiation of pain is usually toward the groin, pubis or isilateral genitalia. It may terminate in the lower abdominal quadrant. In extremely young patients, the passage of renal or ureteral stones generally causes symptoms similar to those of enteric colic, the pain is likely to be more continuous and not accompanied by diarrhea or other intestinal symptoms. Occasionally the passage of stones from the upper tract is manifested by acute symptoms of vesical calculus.

Laboratory examinations are important as the first step in a complete urologic examination. A roentgenogram is taken to ascertain the presence of stone, although the stones characteristic of early childhood are of uric acid composition and are not radiopaque. In older children from 10 to 15 per cent of urinary calculi will not cast a shadow in the roentgenogram. The treatment for urinary calculus in children is usually surgical, but in a few cases ureteral stones will pass following ureteral dilatation. About 90 per cent of all renal stones pass to the bladder and most of these eventually pass from the meatus. Nephrectomy is indicated only when the kidney is totally destroyed or the stone is so large that its removal by nephrotomy would probably result in ultimate destruction of the kidney. Removal of a stone by pyelotomy will often conserve the kidney. Impacted ureteral calculi are easily removed by ureterotomy. Although small soft stones of the bladder may be crushed by lithotripsy, large or hard stones are most successfully removed by cystotomy. The latter is the method of choice because any obstructions to the neck of the bladder may be destroyed through the open wound or the diverticula may be resected.

#### UROGRAPHY

McCrea<sup>30</sup> called attention to the necessity of having a pyelographic medium that can be detected as it regurgitates from the ureter when

<sup>30</sup> McCrea, L. E. A Contrasting Medium for Pyelographic Study, *J. A. M. A.* 93: 987 (Sept. 28) 1929.

used in conjunction with indigo carmine. Sodium iodide, now the most universally used pyelographic medium, cannot be observed when the regurgitated fluid from the ureter is colored by indigo carmine. The following medium has been prepared and is now being successfully employed: sodium iodide, 12 Gm., emulsion of silver iodide 5 per cent, 20 Gm., distilled water sufficient to make 60 Gm. This combination is a thin, watery, creamy white mixture and can readily be detected by the observer watching the ureteral orifice as a bluish cream-colored fluid. The contrasting medium is of advantage in cases of obstruction of the ureter.

Raffo and his associates<sup>31</sup> stated that the combined method of cystoröntgenography was described by one of them for the first time in 1925, one year prior to the publication of the method of Resier.

Their technic is as follows. A catheter of large diameter is introduced into the bladder, the bladder is completely emptied, 30 cc of barium sulphate in thick aqueous suspension is introduced, and then 100, 150 or 200 cc of air or oxygen is injected until the patient complains of slight pain. Before the roentgenograms are taken, the patient is asked to turn once or twice so as to obtain a uniform coating of the vesical mucosa by the opaque medium. The roentgenograms are taken in the usual way. The lesions of the bladder appear either in the form of filling defects or as dense shadows.

The method of Resier, using iodized oil, does not always demonstrate the irregularities plainly because the higher viscosity of the iodized oil prevents its even distribution on the surface of the mucous membrane. Not infrequently roentgenograms are obtained which do not correspond to actual conditions.

Raffo and his associates have used the combined cystoröntgenography for three years with satisfactory results. Since the filling defects and increased opacities indicate only the site and extent of the lesion and do not indicate its true nature, the method should be used only in conjunction with other clinical procedures.

Haret and Fraim<sup>32</sup> reported a case of multiple calculi of the bladder in a man, aged 40. At operation seventeen stones were found, twelve of which were about 2.5 by 2 cm. and five somewhat smaller. A cross-section of one of the larger stones revealed that the central portion of the calculus consisted of a blue-stained, oily substance which on chemical analysis was found to be gomenol stained with methylene blue (methylthionine chloride, U. S. P.). The bacteriologic examination revealed

31 Raffo, Vittorio, and Vallebona, Alessandro. Quelques remarques a propos de la cystoradiographie, *J. de radiol. et d'électrol.* **13** 481 (Sept.) 1929.

32 Haret and Fraim, M. Radiographie de la vessie, une image rare, *Bull. et mém. Soc. de radiol. méd. de France* **17** 229, 1929.

the presence of active staphylococci. Many years previously gomenol had been injected into the bladder and at the same time methylene blue pills were given. It is probable that the air bubbles which formed at the time of the injection of the gomenol became stained with the methylene blue, and later stones formed. The presence of active staphylococci within the oily substance of the stones so many years later dissipates all illusions with regard to the antiseptic value of gomenol.

Trattner,<sup>33</sup> Wright and Barlow<sup>33</sup> stated that the characteristic action of 12 per cent sodium iodide on the ureter consists in a marked increase of tonus, frequently to the degree of spasm which may be either regional or involve the entire organ. Relaxation of the ureter may also occur. In the interpretation of the pyelo-ureterogram, besides the normal anatomic constrictions and dilatations, and the effects of pressure from injection, it is essential to distinguish the functional response of the ureter produced by the sodium iodide solution from that of an organic lesion.

Bergerhoff<sup>34</sup> pointed out that the older method of pyelography in which the contrast medium was brought directly into the urinary passage was not physiologic. Another method has therefore been perfected by which a contrast medium that consists of a combination of urea and of iodine is injected into the cubital vein and is excreted through the urinary system. Not only does this contrast medium facilitate roentgenoscopy, but its elimination reveals the functional activity of the urinary system. Bergerhoff enumerated the cases in which this method of pyelography should be used and also the cases in which it is contra-indicated. Following a description of the mechanism of the injection of the contrast medium and of the roentgenographic technic, he reported several cases that illustrate the great value of the method. He pointed out that this method of pyelography makes it possible for the physician who is not a specialist in urology to diagnose disorders of the urinary system, and consequently it enlarges the field of his activity. Indications for operative treatment can now be more precise than before this technic was perfected.

Béclère, Porcher and Henry<sup>35</sup> experimented with the preparation employed by von Lichtenberg for intravenous pyelography at St. Hedwig's Hospital in Berlin. This preparation consists of an iodized

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33 Trattner, H. R., Wright, H. B., and Barlow, O. W. An Experimental Study of the Action of Sodium Iodide on Excised and Intact Ureters of Dogs, *J. Urol.* **23** 441 (April) 1930.

34 Bergerhoff, W. Die Anwendung der intravenösen Pyelographie in der urologischen Medizin, *Med. Klin.* **26** 232 (Feb.) 1930.

35 Béclère, H., Porcher, P., and Henry, Robert. Premiers résultats de la méthode de Lichtenberg (Pyelo-uretero-cystographie par injection intra-veineuse). *Bull. et mem. Soc. de radiol. med. de France* **18** 79, 1930.



substance derived from pyridine. It is made in the form of a water-soluble powder, it is absolutely nontoxic and its excretion begins within five minutes after the intravenous injection. The roentgenograms taken ten minutes after the injection are not sharp, but they demonstrate clearly the renal pelvis, the ureters and the bladder.

The method has two advantages. It permits of a study of the structure of the renal pelvis, ureters and bladder in all cases in which ureteral catheterization is impossible or contraindicated, and it gives information with regard to the intimate phenomena of urinary excretion.

The technic is as follows. Forty grams of the powder is dissolved in 80 cc of double distilled water. After the addition of 20 cc more of double distilled water, the solution is filtered through a regular filter paper or sterile gauze, is placed for twenty minutes in a water bath, is refiltered and is maintained at a temperature of 37 C. The intravenous injection is performed according to the usual technic (in the vein of the arm) except that after the injection of the first half of the solution (50 cc) there is a three minute wait before the second half is injected.

The roentgenograms are taken fifteen minutes, thirty minutes and one hour and fifteen minutes after injection. The second roentgenogram, as a rule, shows the maximum contrast. In some of von Lichtenberg's cases positive roentgenograms were obtained six and even twenty-four hours after the injection.

Kielluthner<sup>36</sup> has used an iodopyridine compound for intravenous pyelography for the last three months in a series of thirty-four cases. Roentgenograms were taken from ten to fifteen minutes and from twenty to forty minutes later, in case of disturbed renal function they were taken one hour, two hours and several hours later. All roentgenograms were satisfactory, and ill effects did not follow the injection. The method is of special value in cases in which direct pyelography is impracticable, for example, in cases of children, ureteral stones, malformations and certain abdominal tumors. It is contraindicated in bilateral conditions of the kidney and in thyrotoxicosis.

Roth and Wright<sup>37</sup> stated that the iodopyridine compound is neutral is more than 50 per cent soluble in water and contains 42 per cent of iodine. It is an extremely stable chemical compound, and its opacity to roentgen rays is excellent.

Important information was obtained by comparing roentgenograms of a series of cases, and it is suggested that the use of serial changing cassette holders in conjunction with a Potter-Bucky diaphragm might be of great advantage.

36 Kielluthner. Ueber eine neue, aussichtsreiche Untersuchungsmethode an den Harnorganen (Uroselektan), München med Wchnschr 77 276 (Feb) 1930.

37 Roth, E J H, and Wright, H W S. Intravenous Pyelography, Brit M J 1 778 (April 26) 1930.

Ill effects were not observed from the injection. There was a slight increase in the pulse rate and blood pressure and cramping of the anterior muscles of the shoulder in a few cases, but the symptoms always disappeared within fifteen minutes. The method is perfectly safe, even in cases in which there is marked decrease of renal function. The only contraindications are anuria, uremia and gross disease of the liver and kidney.

In Roth and Wright's series of sixty roentgenograms, they noted that the shadow of the left kidney appears slightly less dense than that of the right. They did not succeed, as others have done, in visualizing by roentgenograms the pelvic shadow accurately enough for pyeloscopy. On the roentgenograms, there was a satisfactory shadow after six minutes and in fifteen minutes there was a perfectly clear outline of the whole of the urinary tract.

An iodopyridine compound can also be used as a test of renal function, since it is easily recovered from the urine. On the addition of hydrochloric acid, it forms a heavy white precipitate when the hydrogen ion concentration reaches from 2.8 to 3. Chemical estimation, however, is not always necessary because the specific gravity is a reliable guide of the drug present. It should reach between 1,045 and 1,050 within an hour.

Roth and Wright were able to confirm the experience of von Lichtenberg, according to which, although advanced noninfected hydronephrosis gives an excellent though perhaps delayed shadow, infected or congested pyonephrosis may not give a shadow.

In conclusion, the opinion is expressed that intravenous pyelography by means of an iodopyridine compound, will play an important part in urologic diagnosis, since it is a reliable test of renal function and is a pyelographic contrast medium.

Hryntschak<sup>38</sup> since 1925, has experimented on animals with numerous opaque mediums for the visualization of the parenchyma and pelvis of the kidney. The following criteria were found to be of significance: (1) The opaque medium must be entirely harmless to the renal tissues, (2) it must be nontoxic, (3) it must possess sufficient contrast (iodine or bromide), (4) it must represent a stable preparation (so that iodine or bromide is not liberated in the organism), (5) it should be neutral, soluble in water (to at least 20 per cent) and permit of sterilization by boiling, and (6) it should be excreted in its entirety in the shortest possible time.

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<sup>38</sup> Hryntschak, Theodor. Studien zur roentgenologischen Darstellung von Nierenparenchym und Nierenbecken auf intravenosem Wege. *Ztschr. f. Urol.* **23**: 893, 1929.

The preparations used by Hryntschak were made synthetically. Simultaneously with the intravenous injection of the opaque medium, pituitary extract was administered intramuscularly in order to increase the power of concentration of the kidney, and atropine was given to decrease the peristalsis of the pelvis and the ureters. Good results were obtained, although the method needs further improvement.

The dose of opaque substance injected by Roseno<sup>39</sup> for intravenous pyelography is described briefly. The preparation is called "pyelognost" and is produced by Gehe and Company, Dresden. Sixty-three grams is injected into a normal patient weighing from 50 to 90 Kg, 15 Gm is subtracted for every kilogram of body weight under 50 Kg, and 15 Gm is added for every kilogram of body weight over 90 Kg.

Roseno<sup>40</sup> gave the results of the clinical application of an iodopyridine compound in human beings as follows. Intravenous pyelography is of great advantage in all cases in which the usual pyelography by retrograde injection is contraindicated as, for example, in urethral stricture, atrophy and tuberculosis of the bladder, occlusion of one of the ureters and tuberculosis of one of the kidneys.

Normally the function of the kidney consists in excretion of the urine. This means that after the injection of the opaque medium the substance is excreted so fast that visualization by roentgenograms is not possible. In order to produce greater concentration of the iodine within the excreting kidney, Roseno added urea, which, in this particular instance, served two purposes: it forms a sort of carrier for the iodine, directing it toward the kidney, and it acts as a diuretic in increasing the permeability of the kidney filter.

The idiosyncrasy for iodine is tested (skin test) the day previous to the examination. If such idiosyncrasy is not present the solution (the nature and concentration are not described) is injected intravenously within from five to fifteen minutes. At the time of injection the bladder must be kept full so as to produce stasis in the renal pelvis, thus delaying the excretion of the opaque medium. Roentgenograms are taken immediately, three and five hours after the injection.

There is a sensation of pressure in the head and occasionally in the thorax associated with a feeling of faintness, such as is observed following the completion of the injection. A little later there is a sensation of thirst, sometimes necessitating the taking of fluids. In other instances there is evidence of headaches and slight elevation of temperature occasionally lasting for more than twenty-four hours. All symptoms disappear within forty-eight hours.

39 Roseno, A. Die intravenöse Pyelographie, *Klin. Wchnschr.* 8 1623 (Aug 27) 1929.

40 Roseno, A. Die intravenöse Pyelographie, *Klin. Wchnschr.* 8 1165 (June 18) 1929.

The normal pyelogram obtained after intravenous injection of the contrast medium is different from that obtained from the retrograde injection in that it appears smaller and less distorted. This, in Roseno's estimation, is due to the fact that mechanical distention is entirely absent in intravenous pyelography.

Twelve roentgenograms illustrate the value of intravenous pyelography in various pathologic conditions. In case of complete occlusion of one of the ureters by stone, kinking or tuberculous stricture it is possible to obtain a good visualization of the kidney and a portion of the ureter above the stricture. In stenosis underneath the ureteral ostia (urethral stricture and hypertrophy of the prostate gland) good visualization of the urinary tract is obtained because of the stasis produced by the stenosis. In cases of stones of the kidney and ureter, one may localize exactly the site of the stones and also the type and extent of the stasis proximal to the stone, and obtain at the same time much information concerning the function of the diseased kidney and the opposite normal kidney. In anomalies of the uropoietic system the type and extent of the anomaly of the complications resulting therefrom can easily be determined. In tuberculosis of the kidney, besides impaired "reflektorische" excretion, tuberculous cavities in the region of the calices and parenchyma may be demonstrated.

In cases of renal tumor as well as of renal cyst, the retrograde pyelography is of greater advantage. Intravenous pyelography, because of almost complete loss of excretion, leads here only to poor visualization of the urinary tract. Most of the so-called functional ureteral kinkings and Hunner's ureteral strictures are artefacts, produced probably by manipulation during retrograde pyelography.

Von Lichtenberg and Swick<sup>41</sup> took a pessimistic point of view in a recent consideration of Roseno's work on the value of intravenous pyelography. By this they did not mean to underestimate the idea of intravenous pyelography, but to express doubt that a suitable medium for injection would be found. Yet Roseno, by emphasizing the physiologic and pathophysiologic phenomena, obtained marked results in this respect.

In comparing intravenous pyelography by means of iodopyridine compound with retrograde pyelography, the authors attempted to determine at the St. Hedwig Krankenhaus, aided by Rave roentgenologist, how far the two methods agreed and what practical conclusions could be drawn. Of the eighty-four cases studied, thirty-five were later checked at operation and one at postmortem examination.

In all instances a good visibility of the urinary tract by the roentgen ray was obtained. If a shadow of the kidney was not demonstrable,

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<sup>41</sup> von Lichtenberg, A. and Swick, M. Klinische Prüfung des Uroselectans, Klin. Wchnschr. 8: 2089 (Nov. 5) 1929.

the kidney either was not present, or function was greatly or entirely destroyed. The functional disturbances of the urinary tract could also be studied with great accuracy.

In the 84 cases studied (this number later increased to 160), satisfactory information was obtained concerning the best therapeutic procedure from intravenous pyelography alone in 75 per cent, in the remainder of the cases the examination had to be supplemented by cystoscopy, catheterization of the ureters and pyelography. The functional test as estimated from observations by the roentgen rays likewise led to positive information in 75 per cent of the cases.

Intravenous pyelography is indicated (1) in all instances in which cystoscopy, ureteral catheterization and direct pyelography are contraindicated either for anatomic, pathologic or technical reasons, (2) in all cases of ureteral occlusion, and (3) in all cases in which the application of direct pyelography is associated with certain risk to the patient.

In the cases of limited renal function direct pyelography by the routine procedure, on account of the better contrast, leads to more satisfactory results.

Since 95 per cent of the injected iodine is excreted in the urine within from six to eight hours, it was attempted to find whether the rate and the percentage of the iodine excreted could not be used as a basis of the functional test of the uropoietic system. Three methods were employed for this purpose: (1) the determination of the excreted iodine, (2) the quantitative determination of the excreted iodopyridine compound, and (3) the determination of the specific gravity of the urine, this increasing proportionately with the amount of iodine present. So far it has not been possible to find out which of the three methods would be of practical value.

The association of pyelography with pyeloscopy is indicated also in the intravenous application of the method.

An attempt was made to administer the iodopyridine compound by mouth, but this procedure proved unsatisfactory.

Swick,<sup>42</sup> after a brief description of the procedures which led to the discovery of an iodopyridine compound by Binz and Rath, defined the characteristics of this compound as follows. The iodopyridine compound is nontoxic, soluble in water and neutral in its reaction, and under normal conditions it is excreted as such through the genito-urinary tract within eight hours practically to the extent of from 90 to 100 per cent. The iodine in the molecule exists in a stable, organically bound state, thus explaining why iodism has never been observed. Its

<sup>42</sup> Swick, M. Intravenous Urography by Means of Uroselectan. *Am J Surg* 8: 405 (Feb.) 1930.

tolerance is exceedingly great, theoretically 180 Gm of the substance, in terms of iodine 75.6 Gm, can be administered to a person weighing 60 Kg

A child aged 7 years would receive half the dose and a child aged 2 years a fourth of the dose administered to an adult. The injection is made in two stages, at intervals of from three to five minutes, by using from five to six syringes previously sterilized in distilled water. The first roentgenogram is made fifteen minutes after the last injection, the second about from twenty to thirty minutes after the first roentgenogram and the third a corresponding period after the second roentgenogram. In disturbances of renal function, subsequent films are taken at intervals of from two to four hours.

The reaction consists of thirst and generalized warmth, particularly of the face and region of the bladder, and occasionally of nausea. Shivering and vomiting of short duration occurred in a case of nephrosis. A child aged 10 years died shortly after the injection, but the uremia that had existed a long time previous to the injection was probably responsible.

Intravenous urography is indicated whenever ureteral catheterization is dangerous or mechanically impossible, in cases of infection of the lower part of the genito-urinary tract in the presence of bleeding, in cases of implanted ureters and in the case of children.

Truchot<sup>43</sup> described four cases in which the application of intravenous pyelography led to the correct diagnosis. He used an iodopyridine compound for intravenous pyelography in about twenty examinations of the urinary system. The method of injection was that employed by von Lichtenberg. Ill effects were not observed except for a slight sensation of heat in the head lasting for a period of from ten to fifteen minutes.

The intensity of the shadow of the urinary tract was controlled roentgenoscopically, and roentgenograms were taken at the peak of the visibility of the image.

Ravasin and Gortan<sup>44</sup> have used an iodopyridine compound in ten cases in which the lesions were varied, such as mobile kidney, marked chronic cystitis, bilateral cystopyelitis in pregnancy, bilateral pyelonephrosis, stone in the pelvis of the kidney, double ureters, infected prostate gland, cystopyelitis in pregnancy, nine month pregnancy with constricted pelvis of the kidney and polycystic kidneys. The conclusion

43 Truchot. Presentation de quelques radiographies du système urinaire obtenues après injection intra-veineuse d'uroselectan. Bull. et mem. Soc. de radiol. med. de France **18** 171, 1930.

44 Ravasin and Gortan. Il quadro radiografico delle vie urinarie mediante l'iniezione endovenosa con l'uroselectan. Radiol. med. **17** 327 (March) 1930.

is reached that the preparation is entirely innocuous, in two cases there was temporary elevation of temperature but this was due, as already suspected by von Lichtenberg, to the distilled water. Good roentgenograms of the urinary tract were obtained in all cases in which the renal function permitted sufficient elimination of the opaque salt. The method is indicated in all cases in which pyelography cannot be performed. It also gives certain information of a physiologic character.

Vallery-Radot and his associates<sup>45</sup> stated that Osborne, Sutherland, Scholl and Rowntree, in 1923, used sodium iodide orally and intravenously for the demonstration of the urinary tract roentgenologically. Volkmann, in 1924, after experimenting with lithium iodide, sodium bromide and sodium iodide, arrived at the conclusion that sodium iodide is the most suitable of the three. Von Lichtenberg, in 1924, Lenarduzzi and Pecco, in 1927, and Roseno, in 1929, made further contributions to this subject. The method of Roseno consisted of intravenous injection of sodium iodide in association with urea, the latter acting as a diuretic and thus producing more rapid elimination of the iodine. Roentgenograms were taken within fifteen minutes, three hours and five hours after the injection.

Recently, von Lichtenberg and Swick contributed to the method of Osborne and his associates in introducing an iodopyridine compound. This product, prepared by Binz and Rath, consists of a sodium salt of pyridine with 42 per cent iodide organically fixed. The injection is made in two stages, at intervals of three minutes. The roentgenograms are taken fifteen minutes, forty-five minutes and one hour and fifteen minutes, or in the event of functional disturbance of the kidney, six hours, twenty-four hours and even thirty-six hours after the injection of the opaque medium.

Vallery-Radot and his associates investigated the value of the method of von Lichtenberg and Swick by injecting the iodopyridine compound intravenously into two rabbits and one guinea-pig. The preparation was well tolerated, the maximum tolerance dose being 7 Gm for each kilogram of body weight in rabbits, thus giving a maximum dose of 180 Gm for a human being weighing 60 Kg.

As a result of these experiments on animals, the iodopyridine compound (40 Gm dissolved in 100 cc double distilled water) was injected also into one human being, and roentgenograms were taken one, six, sixteen, twenty-three, forty-one and fifty-seven minutes and one hour and thirty-three minutes after the injection.

It was concluded that the method of von Lichtenberg and Swick leads to good visualization of the calices pelvis of the kidney, ureters

<sup>45</sup> Vallery-Radot, Pasteur, Dalsace, Jean, Nemours-Auguste, and Derot, Maurice. Nouveau procede d'exploration radiologique des voies urinaires, *Presse med* 38 385 (March 19) 1930.

and bladder. It also permits the evaluation of functional disturbances of the kidney. The method marks real progress in the study of renal lesions.

Lotsy<sup>46</sup> stated that the irritation caused by the continuous accumulation of eggs of *Bilharzia* in the submucosa of the bladder, kidney and colon leads to a large round cell infiltration of the contiguous tissues, resulting later in mucous papillomas of various forms. After the lapse of one year the eggs become calcified. He presented numerous cases illustrating the different roentgenologic aspects of papillomas and calcification in bilharziasis of the urinary tract.

The following difficulties are especially emphasized from the point of view of differential diagnosis: (1) possible confusion with calculi of the bladder, ureter and kidney, (2) possible confusion with papillomas or infiltrations of the intestinal tract which project into the region of the bladder, ureter or kidney, and (3) misjudgment of the papillomas and calcifications of the urinary tract in cases in which elongation and tortuosity of the ureters are present.

Definite diagnosis was obtained in most cases by the simple use of compression, evacuation of the bladder and roentgenograms in different views. Lotsy is convinced that the injection of opaque solutions for the purpose of differential diagnosis, as advocated by others, is not necessary.

Sargent<sup>47</sup> reviewed a series of vesiculograms showing about 200 seminal vesicles, and compared them with the clinical data. The series included normal, as well as acute and chronic cases of gonorrheal vesiculitis and tuberculous vesiculitis. He concluded that the vesiculogram is constant and does not vary in normal men nor does it vary from time to time in the same subject as long as the condition of the vesicle remains the same. Partial or total dilatation of the seminal vesicle occurs commonly in cases of chronic vesiculitis of several months' duration. This dilatation is thought to be atonic in nature and is not permanent if the inflammation subsides. Dilatation of the ampulla of the vas deferens or of the ejaculatory duct occurs as the result of organic stricture and when present to any degree remains permanently. Diminution in the cavity of the vesicle is a constant observation in acute gonorrheal epididymovesiculitis and is thought to be due to inflammatory swelling of the vesical wall. It is temporary and disappears with recovery from the disease. Contraction of the wall of the

<sup>46</sup> Lotsy, G. O. Sur les difficultés causées par la bilharziose dans l'examen radiographique des voies urinaires, Bull. et mem. Soc. de radiol. med. de France **17** 232 (July) 1929.

<sup>47</sup> Sargent, J. C. Interpretation of the Seminal Vesiculogram, Radiology **12** 472 (June) 1929.



vesicle, with extreme decrease of the cavity, even to the point of obliteration, occurs as the result of long-standing inflammation, a change that is observed in the vesiculogram in chronic vesiculitis, either of gonorrheal or of tuberculous origin. The vesiculogram reveals abscess of the seminal vesicle, when present, and communication with its cavity. Obstructions of the seminal tract, as well as anomalies of the vas and seminal vesicle are revealed in the vesiculogram.

#### ANOMALIES

Hurt<sup>48</sup> studied at necropsy fifty-one male and fifty female infants. Sixty-three were stillborn; the remainder lived for periods of from a few minutes to twelve days. Anomalies of the urinary tract were observed in five cases. In one case bilateral polycystic kidneys were present, the right kidney weighed 15 Gm and the left kidney, 12 Gm. Both were completely cystic, and the pelves were small. In the second case the cause of death was intracranial hemorrhage and prematurity. There was partial stricture of the left ureter 1 cm above the ureterovesical junction. Mild degrees of hydro-ureter and hydronephrosis were present. The left ureter was 5 mm in diameter, and the right 2 mm. There was definite narrowing of the left ureter about 2 cm below the kidney. Each kidney weighed 6 Gm. In the third infant both kidneys were polycystic, and there was complete stricture of each ureter just below the kidneys. The ureters were patent from the strictures to the bladder, but were delicate and thin-walled. The right kidney weighed 4.2 Gm and the left, 4.7 Gm. The fourth case was that of a stillborn, premature male infant. The urinary anomaly in this case was such as to be incompatible with continuance of life for any length of time. The right kidney and ureter were absent. The left kidney weighed only 2 Gm and appeared to be a fibrous mass, a pelvis was not demonstrable. The left ureter was small and delicate, it was obliterated just below the kidney but was patent from the point of obliteration to the bladder. In the fifth case the patient was a premature girl, aged 10 days. The cause of death was a defect in the interventricular septum. There was almost complete stricture of the left ureter just below the renal pelvis, with marked left hydronephrosis. The pelvis was about five times normal size, and the cortex was considerably thinned. The left kidney weighed 16.3 Gm and the right 10.2 Gm.

48. Hurt, A. S. Anomalies of the Urinary Tract in Infants, *Am J Dis Child* 38:1202 (Dec.) 1929.

# ARCHIVES OF SURGERY

VOLUME 21 DECEMBER, 1930—IN TWO PARTS—PART II NUMBER 6

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## TRANSACTIONS OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

THIRTEENTH ANNUAL MEETING, PHILADELPHIA  
MAY 12, 13 AND 14, 1930

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# EXPLORATION OF THE PERICARDIUM AND DECOMPRESSION OF THE HEART

## REPORT OF CASES

WYMAN WHITTEMORE, M D

BOSTON

The transactions of this society contain few articles devoted to surgical treatment of the heart. Because it is not given to any one surgeon to have many of these cases, it is important for members of this society to report such cases in order that a considerable number of cases may be grouped collectively for individual study. Following this idea, it is my desire briefly to report two cases.

## REPORT OF CASES

CASE 1—A man, aged 22, entered the Beth Israel Hospital, Boston, on Jan 7, 1929. A week previously he had been struck on the left side of the chest by an automobile, and within three or four days pneumonia developed in the left lung.

On entrance to the hospital the temperature was 104 F, pulse rate 120, respirations, 30, and blood pressure, 112 systolic and 56 diastolic. The sputum contained type IV pneumococci. Examination of the blood showed 5,230,000 red corpuscles, 16,000 white corpuscles, and 97 per cent polymorphonuclears. At the end of ten days, the temperature, which had gradually come down to 99 F, began to rise again, and signs of fluid developed in the left side of the lower part of the back. Aspiration thirteen days after entrance obtained pus with pneumococci which proved to be type IV. The empyema was drained the same day and a section of the eighth rib was removed under local anesthesia. Three days later the temperature was normal but the following day it rose to 101 F with a faint pericardial rub. Two days later the patient was seen by a medical consultant, who found definite pericardial friction rub and expressed the belief that suppurative pericarditis would develop. Ten days after operation, roentgenograms of the chest showed "a small amount of fluid present in the left side. There was a triangular area of increased density which merged with the right border of the heart, but did not obliterate it. The lung field was clear. The possibility of pericardial effusion could not be ruled out." Three days later roentgenograms showed "cardiac shadow as of water-bottle shape with the characteristic appearance of a large pericardial effusion." The following day the pericardium was aspirated on both the left and the right side but nothing was obtained. Four days later seventeen days after the operation a roentgenogram showed the cardiac shadow slightly larger than before. The patient seemed to be losing ground gradually with considerable abdominal distress. The abdomen was distended and vomiting occurred two or three times each day.

It was decided that exploration of the pericardium was justified in spite of the fact that nothing had been obtained by aspiration. On February 18, twelve days after the operation for empyema under local anesthesia a section of the fourth costal cartilage on the left was removed, the pericardium was exposed,

and a considerable amount of thin fluid was obtained. It was felt that there was probably a pocket of frank pus somewhere in the pericardium, and so the patient was given ether and a section of the fifth costal cartilage was removed. The opening into the pericardial cavity was enlarged and the pericardium explored. There were many adhesions, both anteriorly and posteriorly, between the heart and the pericardium. Some of these were broken up, and a cavity posterior to the heart containing considerable thin, slightly bloody fluid was opened into. This posterior cavity was drained with a small rubber catheter and the anterior cavity with a cigaret wick. Culture from the fluid contained pneumococci.

The day after the operation the patient's temperature was normal, the respiratory rate was 20 and the pulse rate, 90, all abdominal symptoms had disappeared. His temperature remained normal for the rest of his stay in the hospital, and he was discharged on March 10, thirty-nine days after the operation for empyema, and twenty days after the operation on the pericardium, with both empyema and pericarditis healed.

Three days before discharge, roentgenograms showed dulness in the left part of the chest, the result of a thickened pleura. There was no evidence of fluid. The left side of the heart appeared to be somewhat enlarged, but there was no evidence of pericardial effusion.

Three months after leaving the hospital the patient was allowed to return to work, he has been working steadily since then, and is in normal health.

My reason for reporting this case is that the operation was done in spite of the failure to obtain anything by aspiration of the pericardium. For years thoracic surgeons have been accustomed to explore the pleural cavity when there is good reason to do so, and there is no reason why the pericardial cavity should not be explored with just as much safety as the pleural cavity when there are indications to justify it.

The second case is one of a greatly enlarged heart due to valvular disease, in which it was hoped that cardiolysis would be of benefit.

CASE 2—An American schoolboy, aged 15, entered the Massachusetts General Hospital on Jan. 3, 1930, complaining of weakness and shortness of breath, which had been gradually increasing for the past seven months. There was no history of rheumatic fever or chorea. At the age of 5 he had had measles followed by repeated earaches and a discharging right ear. The ear condition appeared to be cured after tonsillectomy one year later. There had been no subsequent sore throats.

Seven months previous to entrance, a few days after a fall from which he had apparently suffered no ill effects, he noticed a swelling of the feet, ankles and legs while trying on shoes. An hour or so later he became exhausted, and collapsed on arriving home. He remained in bed five weeks, and then resumed activity gradually during three more weeks. At the end of this time he attended a summer camp for one month, where he exercised vigorously in spite of not feeling well. Four months before entrance his feet began to swell again, and he had some shortness of breath and palpitation after being up all day. He was in bed for the next two months, and then attended school for the following month. He did fairly well until one month before coming to the hospital, when he caught a cold, and a nonproductive cough developed, which has continued to the time of writing. Three weeks before I first saw him his face had begun to swell so much that he was unable to open his eyes in the morning. His legs

swelled to his knees if he was on his feet too long, and he became dyspneic on slight exertion. Two weeks before, he began to vomit, and he had vomited nearly everything eaten since.

Physical examination on admission showed a fairly well developed and nourished boy lying flat in bed. There was no pain, the breathing was rapid, and the face was puffy and flushed. The heart was enormously enlarged. There were systolic and diastolic thrills, with presystolic, systolic and rumbling diastolic murmurs of the apex and to and fro murmurs at the base. There was no second sound in the aortic area, but distinct and somewhat accentuated sounds at the pulmonic area. There was marked pulsation in the neck. The blood pressure was 120 systolic and 80 diastolic. The abdomen was tense and distended with some gas and a considerable amount of fluid. There was no edema at the ankles or sacrum.

Laboratory examination on admission showed that the urine was normal. The red blood count was 5,200,000, the white blood count, 19,000. A smear showed polymorphonuclears, 55 per cent, lymphocytes, 36 per cent, without abnormality of any of the cells, the platelets were normal. The stool was normal. The Hinton test gave negative results. The liver function test (brown sulphthaleine) showed from 5 to 10 per cent retention after thirty minutes.

On admission the diagnosis was rheumatic heart disease with pericarditis, possibly adhesive. A roentgenogram of the heart taken at a distance of 7 feet showed "enlargement in all diameters, with the curves of the pulmonary conus and auricles particularly prominent."

An electrocardiogram taken on January 6 showed normal rhythm, rate 100, a tendency to right axis deviation, low voltage.  $QRS_1$ , —38-3,  $QRS_2$ , —4. On January 7, the cardiac consultant gave the opinion that "anasarca with ascites at the age of 15 with evidence of cardiac disease makes the diagnosis of chronic pericarditis involving the mediastinum almost certain." He found involvement of the mitral valve with regurgitation. The size of the heart and electrocardiographic observations also favored a diagnosis of adherent pericardium, presumably rheumatic. He advised the use of digitalis, and mersalyl, 1 cc every three days. The prognosis at that time was poor.

The following day the cardiac consultant said that the condition was "active and chronic heart disease with mitral involvement and undoubtedly chronic pericarditis." He expressed the belief that cardiolysis should be seriously considered. The same day roentgenograms showed no evidence of fluid in the pericardium.

For the following ten days the patient had a widely swinging temperature as high as 103 F, with a leukocytosis of from 12,000 to 20,000. Digitalis was given,  $1\frac{1}{2}$  grains (0.09 Gm) daily, a total of 15 grains (0.97 Gm). Between January 4 and 14 he received 60 grams (3.9 Gm) of ammonium chloride daily. From January 5 to February 7, nine doses of mersalyl, either 1 or 2 cc were given intravenously. On January 10, slight tenderness developed in two joints. Salicylates, 40 grains (2.6 Gm) daily, were given between January 10 and 27. Four blood cultures between January 8 and February 2 were negative. During the first nine days, the generalized edema decreased markedly owing to brisk diuresis. The patient showed a loss of 25 pounds (11.3 Kg). No evidence of active endocarditis was found except as suggested by the fever and leukocytosis. By January 23 the patient had regained 11 pounds (5 Kg) and ascites had been increased. Mersalyl at this time is recorded as having caused an excellent diuresis.

On January 24, consultation was held. Cardiolysis was considered "indicated" but was postponed for two or three weeks more of rest, administration of digitalis and diuretics in the hope that the infection and decomposition would stop.

For the next ten days, edema increased with little or no alleviation by diuretics, and cardiac embarrassment became more marked. The temperature fluctuated between 98.6 and 100 F.

Roentgenograms taken on January 31 showed the heart shadow somewhat increased in diameter across the auricles, with evidence of fluid in the pericardium.

On February 7, in a second consultation it was concluded that the recent increase in unfavorable symptoms and signs warranted operative intervention. This was defined to mean rib resection, with evacuation of pericardial fluid if present, and excision or section of the pericardium if adhesions or a fibrinous pericarditis was found. It was felt that the increase in stasis of the head and the upper extremities, combined with the small paradoxical pulse, favored the diagnosis of pericardial effusion with compression of the great vessels.

The patient was prepared for operation by continued administrations of digitalis, mersalyl and morphine. On February 8, an operation was performed. This was begun under local anesthesia, but within a few minutes the patient became very nervous, and it seemed wise to change to light ether anesthesia. The sternal ends of the third, fourth and fifth ribs were resected, and the portion of the sternum overlying the pericardium was removed. During this procedure it was reported that the blood pressure could not be obtained, but as soon as the bony structures overlying the pericardium were removed it was noted that the heart beat was much stronger, and at this time the blood pressure was reported as 120 systolic and 80 diastolic. This was encouraging. The pericardium was found adherent to the anterior part of the thoracic wall, but when opened, contained no fluid. A portion of the pericardium about  $1\frac{1}{2}$  inches (3.7 cm) square was excised. Exploration of the pericardial cavity revealed dense adhesions between the heart and pericardium around the apex and along the left border. The defect in the thoracic wall was closed by muscle, fascia and skin. The patient stood the procedure well, on return to the ward, the blood pressure was 120 systolic and 80 diastolic. This dropped somewhat but rose to the same height within four hours after operation. Although slightly dyspneic, the patient was fairly comfortable.

The following morning the patient was sitting up in bed reading the news paper, and declared that he felt very much better. Edema of the upper extremities and face had completely subsided, making it difficult to recognize the boy although the swelling in his legs remained. The temperature was 101 F, but it came down to normal during the next five days. On February 14, six days after operation, he was seen by a heart consultant who said that there was slight improvement following the operation, with a fuller pulse, increased blood pressure and less edema of the face. The dependent edema and dyspnea had not changed appreciably. He said that the use of digitalis should be continued,  $1\frac{1}{2}$  grains being administered daily, with more diuretics. Two cubic centimeters of mersalyl administered intravenously might help to make more evident any improvement resulting from the operation. After five days his condition gradually changed for the worse. The temperature remained at 101 F, edema of the lower extremities increased. Because of nausea and vomiting, the daily doses of digitalis were omitted. The urinary output following the administration of mersalyl increased from 20 to 40 ounces (567 to 1,134 Gm). There was no appreciable diminution of edema. From February 15 to 17, the patient grew rapidly worse, dyspnea increased, tracheal râles developed and were audible at a distance. On February 17, the blood pressure dropped to 70 systolic and 40 diastolic, edema increased and the patient was semicomatose. Epinephrine, caffeine and sodium benzoate

were given intravenously. The pulse became stronger. Three hours later the patient died before stimulants could be given. Unfortunately, there was no autopsy.

This case did not show the classic signs of adherent pericarditis, such as retraction with each systole and Broadbent's sign, nor was there a bulging of the pericardial region due to the great size of the heart.

Before undertaking the operation there were great doubts as to the value of cardiolysis in cases of enlargement of the heart, but it was felt that if there was adherent pericarditis associated with hypertrophy of the heart, and if at operation some of the adherent pericardium could be removed in addition to the excision of the ribs and sternum overlying it, there was a possibility of improvement. There can be no question but that there was temporary improvement, the improvement, however, lasting only four or five days. Disappearance of the edema of the face and upper extremities twenty-four hours after operation was encouraging, but although it is always unfair to draw conclusions from an isolated case, it would still seem doubtful whether the operation of cardiolysis is of sufficient value in cases of enlargement of the heart to justify its use in these desperate situations.

#### COMMENT

I have chosen these two cases because I believe that progress in thoracic surgery depends to a large extent on the sharing of failures as well as of successes, for only in reporting and comparing various experiences in this little known field can one form any real estimate of the lasting significance of any new surgical undertaking.



# PERICARDIECTOMY IN THE TREATMENT OF THE PICK SYNDROME

EXPERIMENTAL AND CLINICAL OBSERVATIONS\*

CLAUDE S BECK, M D

AND

R A GRISWOLD, M D

CLEVELAND

## INTRODUCTION

With the advent of asepsis, surgery emerged from the doldrums, where it had stood for centuries, and entered a period of unprecedented activity and advancement. A new era, that of operative development, had suddenly dawned. With bountiful promise for every new endeavor, surgery advanced from the beginning to almost the end of that great period in a mere half century. Within the short span of a surgeon's life this historic development could have been seen in panoramic view. Perfected and diversified as this development has been, surgery of the central circulatory system, of the heart with its pericardium, has not kept pace with the advancement in other fields.

The foundation for the development of cardiopericardial surgery has not yet been completely assembled<sup>1</sup>. This last great "Northwest of Surgery" stands today in a position scarcely more favorable than that occupied by abdominal surgery when the great Mikulicz advocated exploratory laparotomy for obscure abdominal conditions. The idea of exploratory pericardiotomy is greeted, even by surgeons of extensive experience, with surprise and spontaneous disfavor. Physicians, in general, do not believe that removal of the pericardium is worth while in the treatment for the Pick syndrome. Their objections, *a priori*, are: 1. The difficulties of the operation give to it a special hazard. 2. After the adhesions have been separated and the pericardium has

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1. Although surgeons have repeatedly opened the pericardial cavity to atmospheric pressure, the effect of pneumopericardium on the mechanics of the circulation has just recently been studied (Beck, C S, and Cox, W V. The Effect of Pericardiostomy on the Mechanics of the Circulation, Arch Surg 21 1025 [Dec Part I] 1930). Although a number of surgical attempts to relieve stenosis of cardiac valves have been made the physiologic basis for this work is yet to be elucidated. So far as we are aware, determinations of intrapericardial pressure in health or disease, in man or in laboratory animals, are yet to be taken. The first patient ductus arteriosus is yet to be ligated.

been removed, adhesions between the heart and its surrounding structures will surely reform.<sup>3</sup> The fibrosis extends into the cardiac muscle and a simple peeling off and removal of the pericardium would not be followed by a permanent improvement. Add to these objections the uncertainties of diagnosis, and the reluctance of physicians to accept this operation can be accounted for.

Pericardiectomy in the treatment for the Pick syndrome is followed by results nothing short of brilliant. What a pity that the diagnosis is so difficult and so infrequently made clinically! Because of the uncertain recognition of this condition, we champion diagnostic pericardiectomy in selected cases of circulatory failure of obscure cause.

Our investigations on the subject of adhesive pericarditis have been both experimental and clinical. Beginning with the primary purpose of producing the Pick syndrome experimentally and relieving it subsequently by operation, the work as it progressed took on a number of illuminating and, we believe, important aspects.

In this paper the discussion is confined entirely to the condition variously designated as *concretio pericardii*, *synechia pericardii*, *symphysis cardiaca*, *pericarditis chronica adhaesiva* and *callous pericarditis*. The term *adhesive pericarditis* is not always applicable to the condition under discussion. The clinical syndrome described by Pick may occur, as shown by our experiments, without the formation of adhesions between the heart and the pericardium, also, the presence of generalized intrapericardial adhesions is not necessarily associated with the Pick syndrome. The essential feature of the condition is a compression effect exerted on the heart by the contraction of scar tissue. We shall refer to the clinical description of this condition by the term "Pick's syndrome" without reference to the various factors that may have produced the compression effect on the heart.

Conditions in which adhesions exist between the external aspect of the pericardium and its contiguous structures are not discussed in this paper.

A résumé of the literature is given in the excellent articles by Schmieden<sup>2</sup> and Churchill.<sup>3</sup>

2 Schmieden V. Ueber die Exstirpation des Herzbeutels, *Zentralbl f Chir* 1 46 1924. Die Heilung der schrumpfenden Pericardial-Synechie durch Exstirpation des Herzbeutels, *Acta chir Scandinav* 57 268 1924, *Neue Ergebnisse bei der Exstirpation des Herzbeutels*, *Arch f klin Chir* 138 552 1925. *Technique of Cardiolysis Surg Gynec Obst* 43 89-93, 1926. Volhard and Schmieden. Ueber Erkennung und Behandlung der Umklammerung des Herzens durch schielige Perikarditis *Klin Wochenschr* 2 5, 1923.

3 Churchill E. D. Decortication of the Heart (Delorme) for Adhesive Pericarditis *Arch Surg* 19 1457 (Dec) 1920.

## THE PICK SYNDROME PRODUCED EXPERIMENTALLY

Adhesions between the heart and the pericardium can be produced readily by the application of chemical irritants or by mechanical trauma to the epicardium or to the parietal pericardium. These procedures have not resulted in any circulatory disability that is demonstrable clinically. The adhesions produced by these methods consist of bands of fibrous tissue extending from one surface to the other usually without completely obliterating the pericardial cavity and without producing any thickening of the parietal pericardium itself.<sup>4</sup> In a study of the effect of surgical solution of chlorinated soda (Dakin's solution) in the normal pericardial cavity of the dog it was found that the solution produced a profound reaction.<sup>5</sup> This consisted of hemorrhage caused by the erosion of small blood vessels, as the immediate reaction and of generalized adhesive pericarditis sometimes with the development of polyserositis, as a delayed reaction. Death uniformly followed the development of polyserositis. The syndrome of adhesive pericarditis and polyserositis produced by the application of surgical solution of chlorinated soda in the normal pericardial cavity of dogs was exactly similar to the condition described by Pick<sup>6</sup> in 1896, which bears the name of Pick's disease.

The dog was anesthetized by ether or by sodium iso-amylethyl barbiturate injected intravenously. Mechanical respiration was provided by the Erlanger apparatus through an intratracheal tube. A short segment of the left fifth rib was resected subperiosteally and the thorax was opened. Either the solution of chlorinated soda was introduced into the pericardial cavity through an aspirating needle, or the pericardial cavity was opened and irrigated through a catheter. Usually from 50 to 100 cc of the solution was used and this was applied for a period of from fifteen to twenty-five minutes. As soon as the irritant was introduced, the pulse rate became rapid and after a few minutes the fluid became hemorrhagic. A small opening was usually left in the pericardium so that fluid as it formed, could escape and thus prevent the development of cardiac tamponade. The air was expelled from the pleural cavity and the wound was sutured in layers with silk.

During the postoperative period the dogs were examined at frequent intervals. The size of the cardiac shadow was determined by roentgenograms which were taken at constant distances so that fairly accurate comparisons could be made. Venous pressures were determined by the direct method of inserting into the jugular vein an aspirating needle connected to an upright manometer and determining the height of a column of physiologic solution of sodium chloride sup-

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4 Beck, C S, and Moore R L. The Significance of the Pericardium in Relation to Surgery of the Heart, *Arch Surg* **11** 550 (Oct) 1925

5 Beck, C S. The Effect of Surgical Solution of Chlorinated Soda (Dakin's Solution) in the Pericardial Cavity *Arch Surg* **18** 1659 (April) 1929

6 Pick, Friedel. Ueber chronische, unter dem Bilde der Lebercirrhose verlaufende Pericarditis (pericarditische Pseudolebercirrhose) nebst Bemerkungen über die Zuckergussleber (Curschmann), *Ztschr f klin Med* **29** 385, 1896

ported in the tube.<sup>7</sup> Minute volume output determinations of the heart were made by means of the Fick principle. Electrocardiograms were taken with the dog in various positions to show the presence or absence of the shift of the electrical axis of the heart. The formation of fluid in the chest, abdomen and subcutaneous tissues was noted, as was also the weight, the circumference of the abdomen, the respiratory rate, the pulse rate and the condition in general.

Polyserositis did not always develop after this procedure. In some experiments, especially in those in which a small quantity of the solution was introduced, only a mild reaction followed. In other experiments, in which the solution was introduced slowly and over a relatively long period of time, necrosis of the myocardium took place, and the experiment was terminated by intrapericardial hemorrhage. The degree of reaction necessary to produce polyserositis had to be learned by experience, and unfortunately a large number of dogs were used. Under favorable circumstances polyserositis developed from one to three months after the solution was applied to the pericardium. It was our experience that when polyserositis developed, the condition progressively became more marked and death usually occurred within a few days after ascites was clinically demonstrable, unless pericardiectomy was performed. In no experiment did the dog recover spontaneously. In the first experiments we were novices in the performance of the operation for the relief of the condition and we needlessly lost a number of animals with marked polyserositis. It required considerable experience before we appreciated fully the narrow margin of tolerance for operation possessed by the dogs with polyserositis. A small anesthetizing dose of sodium iso-amyl-ethyl barbiturate or the induction of ether anesthesia was sometimes lethal. The anesthetic and the aeration of the lungs had to be observed cautiously and controlled. The operating table was heated. The operation had to be carried out with dispatch.

#### EXPERIMENTS

The following protocols were selected from about fifty experiments, not only to illustrate spectacular cures effected by pericardiectomy, but also to demonstrate certain important considerations in the operation, the pathology of the condition and points of clinical interest in the course of the experiment.

EXPERIMENT 1 (Doc 29-17).—The dog, a female collie, weighed 24 Kg. Oct. 23, 1929. Surgical solution of chlorinated soda was injected into the pericardium.

December 7. The pulse rate was 128 and the venous pressure 40 mm. of water. There was an audible systolic rub. The animal had shown no ascites, cyanosis or other signs of decompensation.

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<sup>7</sup> Easter, I. A. E. *The Clinical Aspects of Venous Pressure*. New York: The Macmillan Company, 1929.

December 11 The operation was repeated. The pericardium was only slightly thickened. It was everywhere adherent to the heart. The adhesions were separated and the pericardium was lavaged with surgical solution of chlorinated soda. This dog was examined at weekly intervals. Venous pressure readings were 0, 28 and 25 mm of water. The pulse rate was never above 136 per minute. No cyanosis or other signs of decompensation appeared.

March 15, 1930 The animal was killed. At autopsy the left lung was found to be adherent to the pericardium. The pericardial cavity was completely obliterated by fibrous adhesions, but the pericardium was not thickened. There was no exudate on the liver and no congestion of the viscera.

*Comment*—This experiment showed that obliteration of the pericardial cavity by adhesions need not produce cardiac disability. Unless the pericardium was thickened and contracted so as to interfere with the expansion of the heart or unless there were firm adhesions to surrounding resistant structures, decompensation did not occur.

EXPERIMENT 2 (Dog 29-6)—A female collie weighing 9.2 Kg. was used.

Aug. 20, 1929 The pericardial cavity was irrigated with surgical solution of chlorinated soda.

October 3 Fluid was present in the abdomen and chest. The subcutaneous tissues were edematous. The pulse rate was 140 per minute. The red blood cell count was 4,984,000. The minute volume output of the heart was 467 cc. This represents about one-fourth the normal cardiac output for a dog of this size. Pericardiectomy was decided on. Sodium iso-amyl-ethyl barbiturate, 0.5 Gm., was given intravenously. The abdomen was tapped and the dog died. Generalized edema of the subcutaneous tissues was present. The right side of the chest contained 210 cc., and the left side 140 cc., of clear fluid. The lungs weighed 85 Gm., they were air containing and showed no edema. The heart seemed to be smaller than normal. The pericardium was thickened and appeared to have shrunk. It was everywhere adherent to the heart by fibrous adhesions. There were no pockets of fluid within the pericardium (fig. 1). The abdomen contained 1,320 cc. of clear fluid. The liver was slightly congested and there was a layer of fibrin between its lobes. It weighed 500 Gm. The spleen and kidneys were not congested.

*Comment*—In this experiment polyserositis and edema of the subcutaneous tissues developed within six weeks after the solution was introduced into the pericardial cavity (fig. 1). The minute volume output of the heart before death was greatly decreased. The pericardium and the heart seemed to be smaller than normal. Undoubtedly pericardiectomy would have relieved the heart of this impediment, as shown by other experiments.

EXPERIMENT 3 (Dog 29-29)—A male mongrel collie weighed 15.3 Kg. Dec. 3, 1929 Surgical solution of chlorinated soda was injected into the pericardial cavity.

December 21 A roentgenogram showed that the cardiopericardial shadow had definitely increased in size. The venous pressure was 170 mm.

December 30 There were no signs of fluid in the chest or abdomen and no edema. The venous pressure was 112 mm. The dog was inactive and had lost its appetite.

Jan 6, 1930 Edema of the scrotum had developed Fluid was present in the abdomen The circumference of the abdomen was 56 cm, the dog weighed 17.2 Kg The respiratory rate was 36 per minute, the pulse rate 180 and the venous pressure 160 mm

January 13 In roentgenograms the cardiopericardial shadow had definitely increased in size The diaphragm was elevated Fluid was present in the chest The animal weighed 17.8 Kg The respiratory rate was 36 per minute, the pulse rate 184 and the venous pressure 220 mm A systolic rub was heard over the left side of the chest The dog was listless and inactive The circumference of the abdomen was 62 cm Electrocardiograms taken with the dog lying on the right side and then on the left side showed a shift of the electrical axis with change of



Fig 1 (experiment 2, dog 29-6) —The heart and the pericardium seemed to be smaller than normal The pericardium was thickened and generalized intra-pericardial adhesions were seen The Pick syndrome was present

position The minute volume output of the heart was 1480 cc (The normal minute volume output of the heart in a dog of this weight is about 2,200 cc) In inserting the aspirating needle through the pericardium and heart for specimens of ventricular blood, definite resistance was encountered in passing the needle through the pericardium

January 16 The weight of the dog was 18.275 Kg The circumference of the abdomen was 68 cm The pulse rate was 172 per minute Respirations were labored, the rate being 44 per minute An operation was performed The subcutaneous tissues and muscles were edematous and the veins of the thoracic all were congested Several inches of the left fifth rib were removed The chest contained 300 or 400 cc of bloody fluid The pericardium was exposed The

heart was pulsating feebly. It was apparent that immediate measures were necessary to free the heart from its encumbrance. We cut through the thickened pericardium and felt with the finger for the plane of cleavage between the heart and the pericardium. Unfortunately, the plane could not be found and the finger dissected into the wall of the left ventricle. After considerable difficulty, the pericardium was dissected free, but at this time the heart was no longer pulsating. Epinephrine was injected into the heart, which was then massaged. A few feeble pulsations were obtained, but they did not become forceful.



Fig 2 (experiment 3, dog 29-29) —Several layers of laminated scar involved both the parietal pericardium and the epicardium. It was impossible, even in the specimen at necropsy, to remove this scar completely without injury to the coronary vessels and the myocardium. The tear in the muscle was made at operation in the attempt to find a line of cleavage.

The specimen was of great interest (fig 2). The adherent pericardium and epicardium appeared similar to those in the human being in certain conditions. These structures were several millimeters in thickness and were definitely laminated. After we had removed from the heart what we considered to be the parietal pericardium there remained another fibrous layer over the surface of the heart, after the latter layer was dissected free there was in places still another

layer intimately involving the coronary vessels and myocardium. It was impossible to remove the entire scar with the scalpel without cutting down to the muscle fibers and the coronary vessels. If attempts at a dissection of this kind were carried out on the pulsating heart, the possibility of cutting coronary vessels would be great. The heart weighed 160 Gm.

Microscopically, the thickened pericardium and epicardium were composed of connective tissue elements compactly arranged. It was everywhere hyalinized and

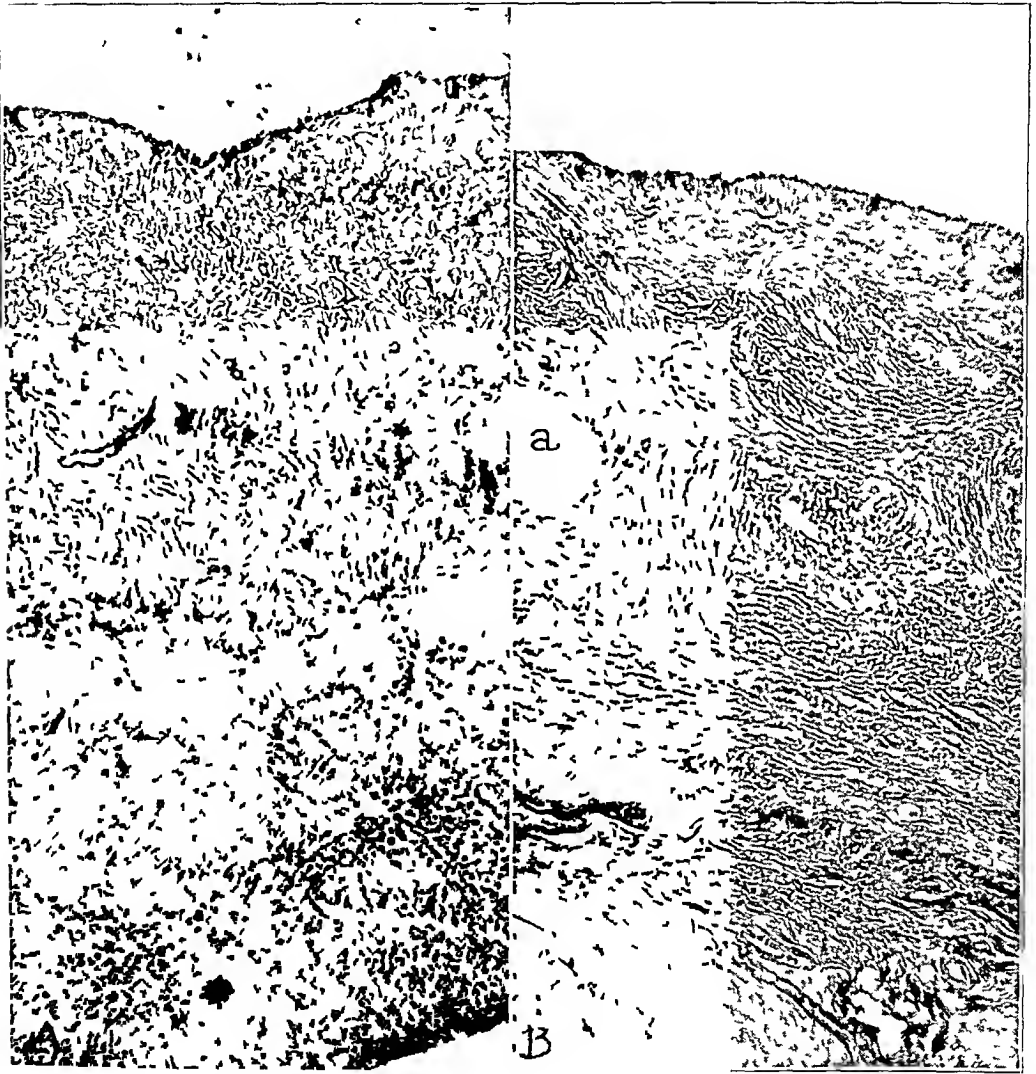


Fig 3 (experiment 3, dog 29-29) —Deposition of scar involving parietal pericardium and epicardium. *A* was separated from *B* at operation. Another plane of cleavage is present in *B* at *a*. The scar did not deeply invade the myocardium appearing at the bottom in *B*, but the coronary vessels were involved in the scar.

contained few blood vessels. There was little, if any, leukocytic infiltration. This hyalinized tissue was intimately adherent to the parietal pericardium and epicardium (fig 3). The scar tissue formation was limited by the epicardium and it did not invade the underlying myocardium.

The lungs were air containing, weighed 130 Gm and showed no edema or consolidation.





Fig 4 (experiment 3, dog 29-29) —On the surface of the liver a thin fibrinous exudate was present, between the contiguous lobes there was a thick deposition of fibrin. These fibrin deposits developed in the course of six weeks. It is probable that had the experiment continued over a sufficiently long period of time the classic "zuckergussleber" might have formed.

The abdomen contained 2,000 cc of straw-colored fluid. The liver was markedly congested and weighed 560 Gm. A point of great interest was the presence of a thin layer of fibrin on the diaphragmatic surface of the liver (fig 4). This fibrinous layer lay in thick plaques between the various lobes of the liver, from which it was easily separated. The fibrin was arranged in laminae and was avascular. Where it was attached to the liver there was considerable infiltration with round cells, but elsewhere it contained only an occasional leukocyte (fig 5).



Fig 5 (experiment 3, dog 29-29) —A laminated exudate of fibrin, devoid of leukocytes and loosely attached to the capsule, was present on the liver

The capillaries around the central veins of the liver were distended with blood, and the parenchyma in these areas contained an increased amount of fat.

The spleen weighed 42 Gm and revealed some congestion. The kidneys weighed 83 Gm and showed capillary engorgement.

*Comment* —Although the pericardium and the epicardium were everywhere scarred and adherent, the electrical axis of the heart shifted with change in position. In this case we failed to relieve the adhesive peri-

carditis by operation chiefly because we delayed operation to the point where death from decompensation was imminent. The dog was waterlogged and there was no cardiac reserve to make the operation successful. Complete resection of the scarred pericardium by sharp dissection was impossible even at necropsy. The involvement of epicardium and coronary vessels with scar was so intimate that the danger of injuring coronary vessels in the dissection was great (figs 2 and 3). This possible danger undoubtedly may exist in certain cases in the human being and may add to the hazard of the operation.

The thickened, leathery pericardium gave a definite sense of resistance to the aspirating needle when the ventricles were tapped for specimens of blood. This sense of resistance could perhaps be utilized clinically in the human being as a diagnostic adjunct in questionable cases of adhesive pericarditis.

EXPERIMENT 4 (Dog 29-35) —A male mongrel weighed 98 Kg. Dec 11, 1929. The pericardial cavity was irrigated with surgical solution of chlorinated soda. A preoperative roentgenogram showed the transverse diameter of the heart to be 6.5 cm and the longitudinal diameter 9.8 cm.

December 24. The general condition was good and there was no evidence of circulatory failure. The minute volume output of the heart was 741 cc. The venous pressure was 90 mm. There were no signs of fluid. The pulse rate was 140 per minute.

Jan 6, 1930. There seemed to be no change, the weight was 88 Kg.

January 13. The weight was 107 Kg. The venous pressure was 210 mm and the pulse rate 156 per minute. There was slight edema of the scrotum and apparently some fluid in the chest and abdomen. Electrocardiograms showed no shift of the electrical axis of the heart with change of position. The circumference of the abdomen was 52 cm. The transverse diameter of the heart was 6 cm and the longitudinal diameter 8.4 cm, as shown by the roentgenogram.

January 16. There was marked ascites and evidence of fluid in the chest. The pulse rate per minute was 158 and the respiratory rate 24. The circumference of the abdomen was 56 cm. The scrotum was edematous. It was decided to make another cardiac output determination before pericardiectomy was carried out. During the cardiac puncture the dog coughed up a little blood and died. At autopsy the chest was filled with bloody fluid and there was a large amount of pink fluid in the abdomen. The soft tissues were edematous and the veins were distended. Both lungs were extensively adherent to the pericardium and there were adhesions to the scar of the thoracic wall on the left side. The pericardio-diaphragmatic ligaments were thickened and tense. The parietal pericardium was everywhere tightly adherent to the heart and in some places could be separated only by sharp dissection (fig 6). Over the right ventricle the myocardium was dark, as though it had been burned deeply with surgical solution of chlorinated soda. The lungs were edematous, and the liver was congested. There was a thin fibrinous exudate over the surface of the liver.

*Comment* —In the light of later experience it would seem that pericardiectomy should have been carried out earlier. The diminution in

the size of the heart in this dog by reason of shrinkage of the pericardium was marked. The fixation of the electrical axis of the heart was explained by the adhesion to the wall of the chest and by the thick tense pericardio-diaphragmatic ligaments, which acted as guy wires, holding the heart firmly in position (fig 6)

EXPERIMENT 5 (DOG 29-5) —A male mongrel police dog weighed 22.2 Kg Aug 19, 1929. Surgical solution of chlorinated soda was injected into the pericardial cavity

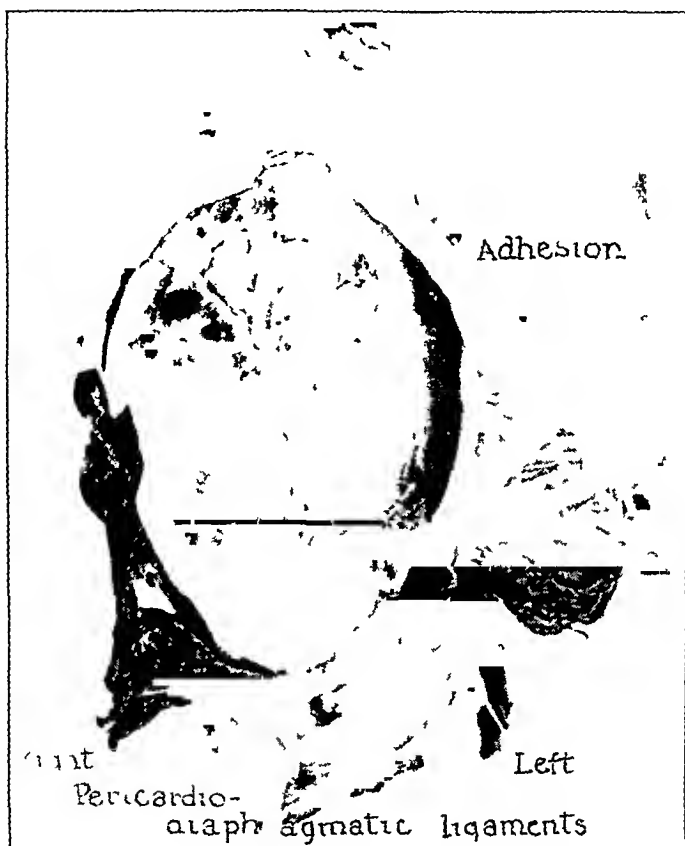


Fig 6 (experiment 4, dog 29-35) —The pericardium is opened and dissected from the epicardium. The adhesion to the chest wall and the thickened pericardio-diaphragmatic ligaments account for the fixation of the electrical axis of the heart with change of position.

October 1. A systolic friction rub was heard over the right side of the chest. The jugular veins were distended. The tongue seemed to be slightly cyanotic. There was no demonstrable ascites or fluid in the chest. The dog weighed 18.4 Kg.

October 12. The abdomen was greatly distended with fluid, and edema of the scrotum and of the paws was present. The cardiac sounds were faint. The rub had disappeared. The tongue was cyanotic and the jugular veins were distended. The chest contained fluid. The pulse rate was 156 per minute and the respiratory rate 20. The temperature was normal, the red blood cell count was 4,480,000.

and the hemoglobin content 60 per cent. The minute volume output of the heart was 1,684 cc (the normal minute volume output for a dog of this size is well over 3,000 cc), 2,260 cc of straw-colored fluid was removed from the abdomen. The roentgenograms showed a large globular heart.

October 15. Marked edema and polyserositis were present. The minute volume output of the heart was 908 cc. Aspiration of the abdominal cavity yielded 540 cc and that of the pericardial cavity 14 cc.

Pericardiectomy was decided on, but the injection of 0.5 Gm of sodium iso-amyl-ethyl barbiturate was followed by the death of the dog. The right side of the chest contained 400 cc, and the left side of the chest 50 cc, of bloody fluid. There was 300 cc of clear fluid in the abdomen. The pericardium was thickened. There were no extrapericardial adhesions. The pericardial cavity contained about 100 cc of clotted blood. There were some fibrinous adhesions between the pericardium and the heart. The lungs were everywhere air containing and showed no edema, they weighed 262 Gm. The surface of the liver was adherent to the peritoneum by fibrinous adhesions, and between contiguous lobes of the liver a well marked fibrinous exudate was present. The liver, spleen and kidneys showed capillary congestion.

*Comment*—The acutely developing cardiac failure in the foregoing experiment was caused partly by the tamponade produced by the blood clot in the pericardial cavity. A marked degree of cardiac decompensation developed. Fluid was present in the chest and in the abdomen. Subcutaneous edema had developed. The minute volume output of the heart was greatly reduced. The cardiac reserve was nil at the time we intended to perform pericardiectomy. This operation should have been performed before the decompensation became marked.

EXPERIMENT 6 (Dog 29-21).—A male mongrel collie weighed 10.1 Kg. Nov 14, 1929. Surgical solution of chlorinated soda was injected into the pericardial cavity.

December 7. The weight of the dog was 12.9 Kg. There was no demonstrable fluid in the chest and no edema of the extremities. The jugular veins were dilated and the venous pressure was 55 mm. Five hundred cubic centimeters of pink fluid was removed from the abdomen.

December 9. The dog was somewhat listless and weak. The minute volume output of the heart was 1,316 cc. (The normal minute volume output for a dog of this weight is about 1,800 cc.)

December 10. Fluid had formed in the abdomen, and it was apparent that an immediate operation was necessary to save the dog. Edema was present in the tissues of the chest and abdomen. The minute volume output of the heart was 1,451 cc. In drawing the samples of blood from the heart it was noticed that a definite resistance was met by the aspirating needle in passing through the pericardium. The abdomen was tapped, and 500 cc of straw-colored fluid was obtained. The dog was placed on a warm operating table, and ether anesthesia was started. The left fifth rib was removed. There was no free fluid in the chest. The lung was found to be adherent in small areas to the pericardium. The pericardium was picked up and incised. It was about 3 mm thick, tough and fibrous. Much to our surprise, the pericardium was not adherent anywhere to the heart. The left phrenic nerve was dissected from the pericardium. The pericardium was then widely resected over each side of the heart, well up over

the auricles. At this point the tube slipped out of the trachea and the anesthetist inserted it into the esophagus. By the time the tube was reinserted into the trachea the heart was at a standstill. After the administration of epinephrine the heart began to pulsate, but the pulsations did not become forceful. Closure was carried out, but by the time the wound was sutured the heart had stopped beating.

The epicardium was covered by a thin film of fibrous tissue, which subsequently might have impaired the diastolic expansion or filling of the heart (fig 7). The heart seemed to be smaller than normal, it weighed 76 Gm. Microscopically, the scar lay entirely exterior to the epicardium, showing no involvement of the underlying elements. The scar of the parietal pericardium was several millimeters thick and showed some infiltration with leukocytes. The lungs weighed 103 Gm and were moderately edematous. Microscopically, a few scattered areas of lobular pneumonia were found, together with well marked congestion. The abdomen contained 200 cc of fluid. The liver was congested and weighed 530 Gm. A fibrinous exudate was present between contiguous lobes of the liver. Microscopically, the surface of the liver showed a fibrinous exudate infiltrated with leukocytes. There was some congestion around the central veins. The kidneys showed some capillary congestion, especially in the glomerular tufts.

*Comment*—This experiment was especially instructive in that the fully developed syndrome of Pick's disease was produced without any adhesions between the pericardium and epicardium. In this case the impediment to the circulation was produced by scar tissue formation in the parietal pericardium, without any adhesions to the heart. Pericardiectomy should have been followed by a beneficial result. Had the epicardial scar (fig 7) continued to increase, however, polyserositis might have developed again.

**EXPERIMENT 7 (Dog 29-36)**—A female mongrel shepherd dog weighed 18.6 Kg. Dec 11, 1929. The pericardial cavity was irrigated with surgical solution of chlorinated soda.

December 18. The minute volume output of the heart was 2,366 cc.

December 21. The venous pressure was 110 mm and the weight of the dog 20.8 Kg. Respirations were labored, the pulse was rapid, and there was some dullness over the right side of the chest. A roentgenogram showed haziness and increased density (fluid).

December 23. Respirations were labored, and the dog appeared sick. The minute volume output of the heart was 2,524 cc. There was clinical evidence of fluid in the chest. No abdominal fluid could be demonstrated. There was superficial infection of the previous incision. Ether anesthesia was administered and the left fifth rib resected. There was about 500 cc of serosanguineous fluid in the chest. The pericardium was tense, leathery and discolored by hemorrhage. It was incised from the apex to the base. There was no free pericardial fluid, though in some places organizing clots were found. The adhesions, which were present everywhere over the heart, were easily separated. The left phrenic nerve was dissected free and the pericardium excised on both sides as far as possible. The heart seemed to dilate as the restricting pericardium was removed, and the color of the tissue improved. The fluid was removed from the chest, and the wound was closed in layers with silk. On the following day the animal seemed to be in better condition, more active and bright. The pulse rate per minute was 164.

December 26 The pulse rate per minute was 156 and the respiratory rate 36, respirations were somewhat labored but better than before operation The venous pressure was 68 mm of water The dog was stronger, not so listless and eating well Later in the day, it was noticed that the wound had broken open into the pleura, probably as a result of the infection in the wall of the chest from the previous operation It was closed at once, but showed little tendency to heal

Jan 4, 1930 Death occurred from infection Necropsy showed empyema and epicardial infection The remaining fringes of pericardium were adherent to the heart The abdomen contained no fluid and there was no exudate between the lobes of the liver

*Comment*—Failure in this case was due to the occurrence of infection The early postoperative course, with marked improvement in the

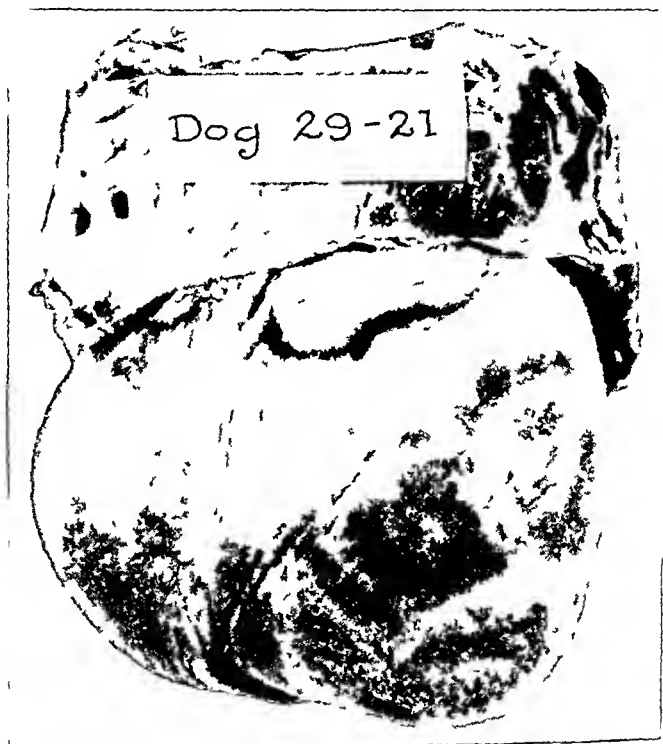


Fig 7 (experiment 6, dog 29-21) —The pericardium was resected at operation It was thickened but nowhere was it adherent to the heart The heart seemed to have been compressed by the shrinking of the parietal pericardium Resection of the pericardium undoubtedly would have been followed by improvement in the circulation The epicardium was glazed with a film of scar tissue which subsequently might have thickened sufficiently to impair the filling of the heart

general condition and a marked fall in the venous pressure, indicated that the operation was effective, and that the circulation would have improved if the infection had not occurred

EXPERIMENT 8 (Dog 29-31) —A male collie weighed 19.5 Kg Dec 5, 1929 Surgical solution of chlorinated soda was injected into the pericardial cavity

December 21 The cardiopericardial roentgenogram was larger than normal measuring 9.4 cm in the transverse diameter The venous pressure was 130 mm

December 24 The dog was so weak that it could not stand. Respirations were labored. Cyanosis of the tongue was present. The pulse was rapid and weak. Eight hundred cubic centimeters of pink fluid was tapped from the abdomen and 200 cc of bloody fluid from the chest.

December 26 The soft tissues over the abdomen and chest were markedly edematous. Dyspnea and cyanosis were marked. The pulse was scarcely perceptible, its rate being about 200 per minute. The dog was placed on a warm operating table and anesthetized with ether. The left fifth rib was removed and the chest was opened. Four hundred cubic centimeters of bloody fluid was removed from the chest. The heart was at a standstill. Epinephrine was injected into it, and it began to pulsate feebly. The pericardium and its contents appeared dark, resembling liver. The lung was adherent to the pericardium and was congested. An incision was quickly made into the pericardium, which was several millimeters thick, tense and adherent to the heart. A line of cleavage was found, and with the finger the pericardium was freed from the heart. Several pockets of bloody fluid were evacuated during this procedure. The heart seemed to dilate slightly after it was dissected free from the pericardium, but its pulsations were feeble. We quickly excised the pericardium, and in our haste we sacrificed the left phrenic nerve (fig 8). The tongue of lung that was adherent to the pericardium was ligated and excised. As closure was carried out, the color of the tissues seemed to improve. We feared that the operation would not save the dog.

December 31 The shadow of the heart, as shown by a roentgenogram, measured 8.4 cm in the transverse diameter. This represented a decrease of 1 cm from the measurement made before operation, this difference undoubtedly could be accounted for by the presence of small pockets containing clotted blood between the heart and the pericardium.

Jan 3, 1930 Edema of the tissues persisted. The pulse rate was 164 per minute and the respiratory rate 30. The venous pressure was 105 mm. The circumference of the abdomen was 61 cm. The dog was able to walk and showed improvement as compared with its condition immediately before operation.

January 6 The dog had undergone striking improvement. The subcutaneous edema had completely disappeared. The ascites was much less, the circumference of the abdomen was 56 cm. Respirations were not labored, the rate being 24 per minute, the pulse rate was 140, the venous pressure 80 mm and the weight of the animal 19 Kg.

January 13 The dog was very active, the pulse rate was 160, but this rapid rate was caused by excitement. The appetite was good. The venous pressure was 70 mm.

January 20 The dog was active, the venous pressure was 65 mm, the pulse rate 144 per minute and the respiratory rate 18. The weight of the dog was 19.2 Kg and the circumference of the abdomen 62 cm. Fluid was forming in the abdomen. Slight edema of the scrotum was present.

January 27 The venous pressure was 170 mm.

February 10 The weight was 21 Kg. The circumference of the abdomen was 71 cm. The pulse rate was 156 per minute. The abdomen was distended with fluid. The venous pressure was 240 mm. Eighteen hundred cubic centimeters of fluid was tapped from the abdomen. The shadow of the heart in roentgenograms measured 7.7 cm in the transverse diameter. A shadow was present over the right margin of the heart. We concluded that the portion of the pericardium over the venae cavae that could not be resected at the previous operation was producing the circulatory failure that had been developing since January 20. The exposure through the left side of the chest was inadequate for the complete resection of



the pericardium in the region of the venae cavae. We interpreted the decrease in the size of the cardiac shadow in the roentgenogram as being due to the formation and contracture of epicardial scar. The electrocardiograms showed no shift in the electrical axis of the heart with change of position. The dog was placed on a warm operating table, and ether was administered. The right fifth rib was



Fig 8 (experiment 8, dog 29-31) —*A*, segments of parietal pericardium excised from the left side of the heart at the first operation. *B*, segments of parietal pericardium excised from the right auricle and ventricle at the second operation. The importance of complete excision of the scar was emphasized.

resected and the chest was opened. There was no fluid. Mediastinal fat was adherent to the heart on the right side. This was sufficient to prevent shifting of the heart with change of position. A segment of pericardium was found adherent to the right auricle and the venae cavae, also extending over a small area of the

right ventricle The parietal pericardium was dissected from these structures by the finger As the inferior vena cava was approached, a broad band of thickened scar was found extending from the parietal pericardium between the vena cava and the auricle This scar produced partial obstruction to the vena cava (fig 9) The band was incised and its pedicle ligated When it was released, it disappeared from view A segment of pericardium equivalent to 30 sq cm was resected (fig 8) The epicardium was covered with fibrous tissue The right phrenic nerve was involved in the pericardial scar, and it was accidentally sacrificed At the completion of the operation the respiratory movements were costal, each phrenic nerve having been sacrificed

February 20 The paralysis of the diaphragm greatly interfered with respiration The dog had undergone a remarkable improvement since the last operation,

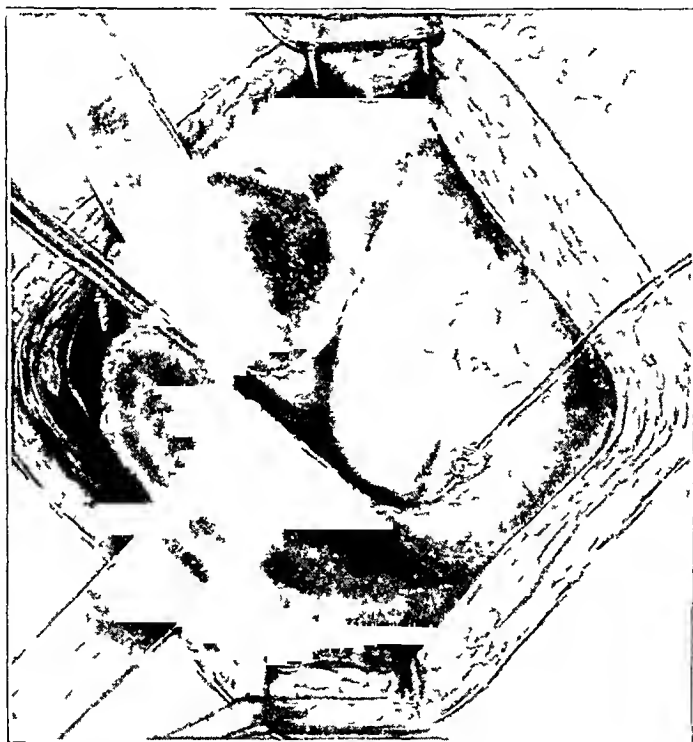


Fig 9 (experiment 8, dog 29-31) —Appearance of the scar that impaired the filling of the right side of the heart and partially obstructed the inferior vena cava The failure to resect this scar at the first operation and the subsequent contracture of it brought about the recurrence of the Pick syndrome

but circulatory embarrassment persisted The pulse rate was 120 per minute The venous pressure was 125 mm Seven hundred cubic centimeters of fluid was tapped from the abdomen The cardiac shadow in the roentgenogram measured 7.5 cm in the transverse diameter The heart had undergone a progressive decrease in size since December 26, when pericardiectomy was performed This was interpreted as due to the formation and contraction of epicardial scar On each side the diaphragm was elevated and encroached on the pleural space

March 6 The venous pressure was 130 mm

March 7 Death occurred The subcutaneous tissues showed slight edema The chest contained 2,000 cc of fluid that looked like a mixture of chocolate and

milk This fluid had a specific gravity of 1.014, contained much fat and many lymphocytes and was not infected. It resembled lymph from the gastro-intestinal tract. The heart was free in the mid-chest and was not adherent to any of the surrounding structures. The heart was "iced" with a film of epicardial scar (fig 10), which undoubtedly had impaired its function. Microscopically, the scar tissue consisted of fairly dense connective tissue elements containing areas that stained blue with hematoxylin and resembled tissue containing calcium. There was no infiltration or fibrosis of the adjacent muscle fibers, but here and there was a deposition of fat. The parietal pericardium removed at operation was less densely organized. It contained many blood vessels and deposits of fibrin. The lungs were edematous and microscopically showed considerable fibrosis. The



Fig 10 (experiment 8, dog 29-31) —The parietal pericardium had been removed at operation. This specimen shows the heart with its encasement of epicardial scar. Although this epicardial scar was adherent to the myocardium, it was possible to dissect it with the scalpel without injury to the myocardium and coronary vessels.

abdomen contained 2,500 cc of pink fluid with a specific gravity of 1.020. The liver weighed 950 Gm, it was markedly congested. The contiguous surfaces of the various lobes of the liver showed an exudate of fibrin, in places 2 mm thick. Each kidney weighed 80 Gm and showed marked venous and capillary congestion.

*Comment* —The foregoing experiment brought out several important considerations. A marked degree of polyserositis and subcutaneous edema developed and it was feared that the cardiac reserve was too

small to tolerate pericardiectomy. The pericardium was separated and excised while the heart was at a standstill. The exposure through the left side of the chest was inadequate to permit complete resection of the pericardium. The region where the venae cavae entered the right auricle was inaccessible through this exposure. A striking improvement followed the operation. During the succeeding three weeks, however, decompensation developed. An operation was again carried out. An exposure was made through the right side of the chest. A segment of thickened pericardium was found adherent to the heart where the venae cavae entered the right auricle, and a band of thickened pericardium caused a partial obstruction to the inferior vena cava (fig 9). The fact that no shift of the electrical axis occurred with change of position was readily accounted for by the adhesions between the right auricle and adjacent structures. This portion of the pericardium was excised (fig 8) and the circulation again improved. During the following month the size of the heart, as shown by roentgenograms, progressively decreased and decompensation again developed. A thick layer of fibrous tissue had formed over the epicardium, this epicardial scar embarrassed the circulation as did the parietal pericardium which had been excised at the preceding operations (fig 10).

The advantage of a bilateral exposure of the pericardium at operation was emphasized in this experiment. The subject will be discussed more fully.

The probable explanation of the decompensation is as follows. During the first period of decompensation, fluid was present in the chest and the lungs were congested. This may have indicated an impairment in the filling of the left side of the heart. The ascites and subcutaneous edema that were also present may have indicated an impairment in the filling of the right side of the heart. The first pericardiectomy relieved the left side of the heart, and pulmonary edema and hydrothorax were absent during the second period of decompensation. The impairment to the filling of the right side of the heart was relieved temporarily by the second pericardiectomy. Then contraction of epicardial scar occurred. The heart decreased in size. The filling of the heart again became impaired, and there was evidence of both right-sided and left-sided failure. This is an excellent example of the effects on the dynamics of the circulation brought about (1) by a generalized restriction to cardiac function (2) by restoration of the left side and restriction of the right side (3) by restoration of the right side and (4) by subsequent bilateral restriction of the heart and failure of both ventricles.

The development of epicardial fibrosis which produced the third instance of decompensation in this experiment has certain clinical

interest One of the deep-seated objections held by physicians to this operation is that even though the pericardial scar can be excised, scar tissue will form again on the epicardium The objection was valid in this experiment The heart, however, did not become adherent to any of the surrounding structures even though an active process of fibrosis was taking place on its surface It was noteworthy, however, that this epicardial scar could be dissected from the myocardium, while it may have been a difficult and hazardous dissection on a pulsating heart, we had the impression that it could have been done successfully (fig 10)

EXPERIMENT 9 (Dog 29-25) —A female collie weighed 17 Kg Dec 2, 1929  
Surgical solution of chlorinated soda was injected into the pericardial cavity

December 24 The minute volume output of the heart was 1,517 cc

December 28 The minute volume output of the heart was 1,326 cc

December 30 The abdomen seemed to be enlarged The venous pressure was 80 mm There were no signs of fluid in the thorax and no edema of the subcutaneous tissues The pulse rate was 120 per minute The electrocardiogram showed a questionable shift of the electrical axis with change of position

Jan 6, 1930 The abdomen was enlarged The mammary glands were hypertrophied, but did not contain milk It was thought that the enlargement of the abdomen was due to pregnancy A few cubic centimeters of fluid was tapped from the abdomen The venous pressure was 75 mm The pulse rate was 140 per minute

January 9 The dog was listless The pulse rate was 152 per minute and the respiratory rate 36 The venous pressure was 375 mm The minute volume output of the heart was 1,339 cc A definite resistance to the passage of the aspirating needle through the pericardium was encountered Again only a few cubic centimeters of fluid could be aspirated from the abdomen, and the increase in the size of the abdomen was believed to be due to pregnancy The cardio-pericardial roentgenograms showed a decrease in size and definitely globular shape (fig 11) This globular contour was interpreted as due to shrinkage of the pericardium The compression thus produced on the heart caused it to assume a more globular shape

January 10 The dog was placed on a warm table and ether anesthesia was given The left fifth rib was removed and the chest was opened There was no fluid A few adhesions were found between the left lung and the pericardium The pericardium was globular and tense, as though distended by its contents An incision was made in it, in doing this a small coronary vein was cut The pericardium was several millimeters thick Adhesions everywhere tightly bound the pericardium to the heart These were separated by blunt dissection The left auricular ear was adherent to the ventricle The left phrenic nerve was dissected from the pericardium as was also the adherent lung The parietal pericardium was then almost completely excised The epicardium did not seem to be scarred The heart throughout tolerated the procedure well There was no bleeding from its surface The wound was sutured

January 27 The dog was active and in good condition It had had puppies a week before The pulse rate was 128 per minute and the respiratory rate 16 The venous pressure was 55 mm

February 10 The venous pressure was 50 mm A roentgenogram showed that the heart had returned to normal in size and shape It was now elongated and somewhat larger than before the pericardium was resected (fig 11)

March 3 The minute volume output of the heart was 1,759 cc The weight of the dog was 12.8 Kg The sense of resistance previously obtained as the aspirating needle penetrated the parietal pericardium was not noted The pulse rate was 108 There was no edema

April 2 The animal weighed 14.2 Kg, it was in good condition and active, with a good appetite The venous pressure varied from 10 to 20 mm There was no evidence of circulatory abnormality

May 1 The dog was in excellent condition The venous pressure was 20 mm The size and shape of the heart appeared the same as in the previous roentgenogram

Microscopically, the parietal pericardium consisted of hyalinized connective tissue containing few cells and measuring about 2 mm in thickness The surface of this scar in contact with the heart possessed a layer of loose areolar tissue which may have allowed slight movement between the heart and the scar

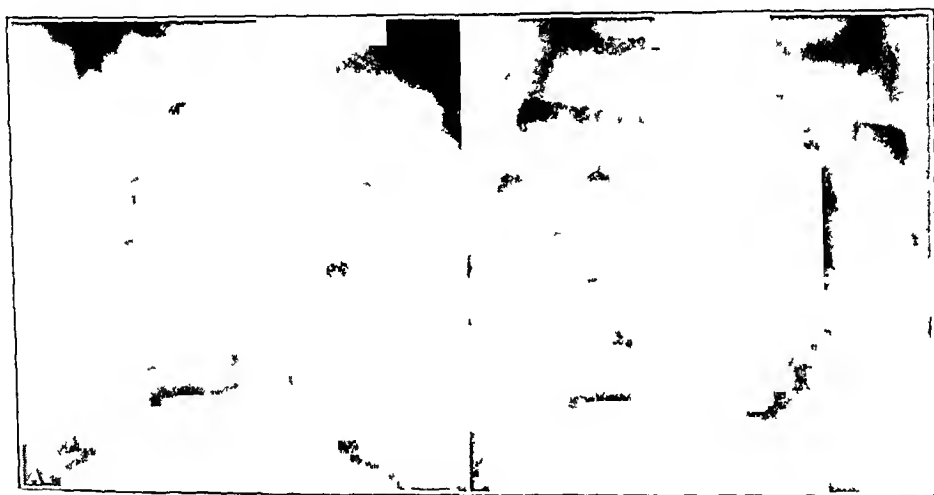


Fig 11 (experiment 9, dog 29-25) —Roentgenograms showing the change in contour of the heart brought about by shrinkage and thickening of the pericardium *A* represents the condition after pericarditis was produced The heart is globular and somewhat smaller than normal *B* represents the condition after pericardiectomy The heart is elongated and has assumed its normal size and contour

*Comment* —In this experiment the injection of surgical solution of chlorinated soda into the pericardial cavity was followed by generalized adhesive pericarditis The condition had not progressed sufficiently long to produce polyserositis The roentgenograms showed that the cardiopericardial shadow had decreased in size and had assumed a globular shape (fig 11) This undoubtedly was caused by shrinkage of the pericardium and compression of the heart Because of this compression the filling of the heart was impaired, the venous pressure increased and the cardiac output decreased Pericardiectomy restored the dog to good health The heart assumed its normal size and shape

The venous pressure fell to normal. The improvement following the operation was progressive and there was no evidence of epicardial scar formation. The heart was not displaced by adhesions. The electrocardiogram showed a shift in the electrical axis with change in position. There was no evidence of myocardial involvement.

EXPERIMENT 10 (DOG 29-43)—A female mongrel bulldog weighed 167 Kg Jan 17, 1930. The pericardial cavity was irrigated with surgical solution of chlorinated soda.

January 27. The dog was active and seemed to be in good condition. It weighed 148 Kg. There was no evidence of decompensation. The circumference of the abdomen was 42 cm. The pulse rate was 180 per minute and the venous pressure 67 mm.

February 10. Polyserositis was developing. The circumference of the abdomen was 51 cm. The animal weighed 16 Kg. The pulse rate was 164 per minute and the respiratory rate 16.

February 21. The venous pressure was 260 mm. The circumference of the abdomen was 63 cm, 900 cc of straw-colored fluid was tapped from the abdomen and the weight after tapping was 177 Kg. Fluid was present in the chest. The cardiopericardial shadow, as seen in roentgenograms, had increased in size.

February 22. The dog was very weak. The tongue was cyanotic. Edema developed in the subcutaneous tissues, especially in the neck. We feared that the dog could not live another day, and an operation was immediately carried out. The animal was placed on a warm operating table and anesthetized with ether. As the incision was made in the thoracic wall, we noticed that there was no bleeding. Pulsation of the heart could not be felt. The chest was quickly opened and the free fluid mopped out. The heart was at a standstill. Epinephrine did not revive the heart, and the situation looked hopeless. The pericardium was tense and thickened. An incision was made into it, and the myocardium to which the pericardium was adherent was also cut. The wound in the heart bled profusely. The plane of cleavage between the thickened pericardium and the heart was found by the finger. In places sharp dissection was necessary to cut these adhesions. Several walled-off pockets of bloody fluid were encountered and opened. They contained approximately 75 cc of fluid. After the adhesions were separated, the heart began to pulsate feebly. The wound in the heart was then sutured, and epinephrine was injected into the myocardium. The pulsations became stronger, and after a while were forceful. The left phrenic nerve was dissected from the pericardium. The pericardio-diaphragmatic ligaments were incised, the mediastinum was dissected from the pericardium and a wide excision of the pericardium was carried out on each side of the heart. Exposure of the region where the venae cavae entered the right auricle was difficult. The pericardium measured about 3 mm in thickness. The fluid was removed from the chest, and closure was carried out. The dog underwent a most spectacular improvement.

March 6. The dog was active. The edema of the subcutaneous tissue seemed to have disappeared. There may have been a little fluid in the abdomen. The cardiopericardial shadow in the roentgenograms was of normal size. The venous pressure was 60 mm. The pulse rate was 136 per minute. The weight was 142 Kg, the dog had lost several kilograms by diuresis.

March 19. The dog was in excellent condition. The venous pressure was 25 mm. The weight of the animal was 136 Kg. There was no evidence of fluid in the chest or the abdomen.

May 1 The venous pressure was 20 mm The dog was in good condition and apparently normal in all respects

*Comment*—In this experiment the introduction of surgical solution of chlorinated soda into the pericardial cavity was followed by a profound degree of circulatory decompensation The heart was at a standstill when pericardiectomy was carried out The parietal pericardium was separated from the heart and several walled-off pockets containing blood-stained fluid were evacuated The heart then began to pulsate, at first feebly, then it made a heroic response Resection of the pericardium was carried out

Following this operation a spectacular improvement took place The dog became active All signs of circulatory failure disappeared The venous pressure decreased to normal The edema and the fluid in the chest and the abdomen disappeared and did not reform As far as could be determined, the dog was restored to normal health When it was last observed, there were no signs of epicardial scar formation, fixation of the heart or myocardial weakness

EXPERIMENT 11 (DOG 29-34)—A male bulldog weighed 16.3 Kg Dec 6, 1929 The venous pressure was normal (0) The cardiopericardial shadow seen in roentgenograms measured 8 cm in its greatest transverse diameter Surgical solution of chlorinated soda was injected into the pericardial cavity

December 21 The cardiopericardial shadow measured 8.7 cm in its greatest transverse diameter The venous pressure was 105 mm There were no signs of decompensation

December 26 The minute volume output of the heart was 1,704 cc

December 28 The minute volume output of the heart was 1,693 cc The dog cooperated perfectly for determinations of cardiac output Definite resistance was encountered by the needle in penetrating the pericardium

December 30 The venous pressure was 50 mm There was no evidence of decompensation

Jan 6, 1930 The venous pressure was 85 mm The pulse rate was 128 per minute and the respiratory rate 18 The animal weighed 16.6 Kg The abdomen seemed to be a little distended, the circumference was 53 cm

January 10 The dog was listless and weak (fig 12) Fluid was present in the abdomen, the circumference was 64 cm The liver was enlarged Fluid was present in the chest Edema of the scrotum was present The venous pressure was 190 mm The pulse rate was 168 per minute and the respiratory rate 21 The electrocardiogram showed a shift of the electrical axis with change of position The minute volume output of the heart was 1,107 cc A definite resistance to the passage of the aspirating needle through the pericardium was encountered

January 11 The cardiopericardial shadow in roentgenograms measured 8.5 cm in its greatest transverse diameter The abdomen was tapped and 600 cc of straw-colored fluid was removed The dog was placed on a warm operating table and ether was given The left fifth rib was resected The chest contained about 400 cc of blood-tinged fluid The lung was not adherent to the pericardium or to the scar in the chest The left phrenic nerve was dissected from the surface



of the pericardium. The pericardium, which appeared dark, was picked up in forceps and incised. It was several millimeters thick and was tightly adherent to the heart. There were no pockets of fluid. A line of cleavage was found and the parietal pericardium was everywhere separated by the finger. The heart seemed to dilate and to fill better as soon as this was done. Incision of the pericardio-diaphragmatic ligaments freed the pericardium. The left pulmonary veins, the inferior vena cava, the ventricles and the base of the heart were freed from the pericardium. The excision of the parietal pericardium was almost complete. A fibrinous plaque, about 5 cm in diameter and 4 mm thick, lay over the

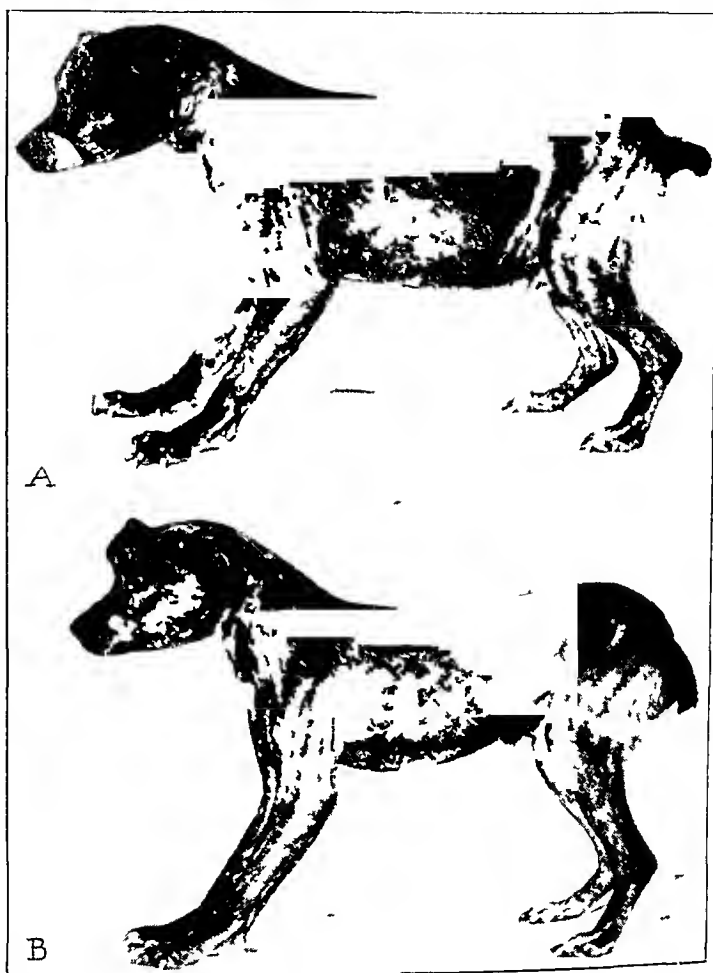


Fig 12 (experiment 11)—*A* was taken before pericardiectomy was performed. The abdomen was distended with fluid and the dog was weak. *B* was taken five days after pericardiectomy and a paracentesis yielding 600 cc

right auricular appendage. The surface of heart now appeared roughened and dark. There seemed to be no scar tissue left on the heart. After the heart was liberated from the pericardium it beat forcibly. We were then able to proceed slowly and carefully with the operation. After the operation the dog weighed 16.7 Kg. It was wrapped in warm blankets. Microscopically, the tissue removed consisted of connective tissue elements in various stages of organization. In places these were compact and took a deep blue stain with hematoxylin. In other places the organization was less compact, showing a lacework of fibroblast fibrin and red blood cells.

January 16 The dog seemed to have undergone remarkable improvement (fig 12) Diuresis followed the operation The polyserositis and edema seemed to have disappeared completely The animal weighed 13.05 Kg

January 20 The circumference of the abdomen was 46 cm and the weight of the dog 13.1 Kg The pulse rate was 110 per minute and the respiratory rate 16 The venous pressure was 25 mm The dog was active and had a good appetite The minute volume output of the heart was 2,502 cc

January 27 The dog weighed 13.4 Kg and was in excellent condition The pulse rate was 100 per minute The electrocardiogram showed a slight shift of the electrical axis with change in position There was less slurring and notching of the Q R S complex, and R showed an increased voltage These changes indicated an improvement of the myocardial function

March 6 The venous pressure was 30 mm, the pulse rate 104 per minute and the weight of the animal 13.3 Kg There were no cardiac murmurs The minute volume output of the heart was 3,528 cc The resistance to the passage of the aspirating needle previously noted was not observed

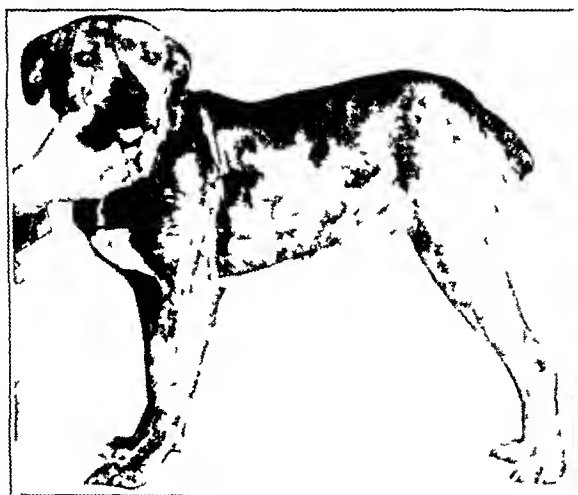


Fig 13 (experiment 11) —Three months later, the dog appeared normal

March 19 The venous pressure was 10 mm There was no evidence of polyserositis or edema The weight was 13.6 Kg

May 1 The dog was in excellent condition The venous pressure was 25 mm The electrocardiogram showed a higher voltage and no slurring, it indicated a normal myocardial function

*Comment*—In this experiment generalized adhesive pericarditis and thickening of the pericardium occurred This was followed by the development of polyserositis and subcutaneous edema (fig 12) The venous pressure rose from 0 to 190 mm and the cardiac output per minute fell to 1,107 cc As soon as the pericardium was separated from the heart, a striking improvement in the circulation took place The heart seemed to dilate as it was freed It filled better, and it beat more forcibly Following the operation all evidence of decompensation disappeared Diuresis took place, the subcutaneous edema and the fluid

in the chest and the abdomen disappeared. The venous pressure fell to 25 mm. The cardiac output per minute rose to 3,528 cc. The general condition of the dog on May 1, 1930, was excellent (fig 13). As far as could be determined, the dog showed no circulatory abnormality. There was no evidence of epicardial scar formation, no fixation of the heart, no adhesions to surrounding structures and no myocardial involvement.

#### COMMENT ON THE EXPERIMENTS

The essential factor in the production of Pick's disease, as can be seen from the experiments, is fibrosis and contracture of the parietal pericardium or epicardium, or both, forming a casing of scar which compresses the heart and primarily obstructs its filling, interfering with cardiac motion as a tightly fitting glove impairs the free movement of the hand. Generalized adhesions between the epicardium and the parietal pericardium are not sufficient in themselves to produce polyserositis. Such adhesions can be produced experimentally, and similar conditions are found clinically in which polyserositis does not develop. Nor is the presence of generalized adhesions necessary for the development of polyserositis. A marked degree of polyserositis developed in one experiment in which there were no adhesions to the heart.

Coincidentally with the development and contracture of scar tissue about the heart, the clinical manifestations of the Pick syndrome in the order of their appearance are: (1) a rise in the venous pressure, (2) ascites and the development of a fibrinous exudate on the liver, (3) hydrothorax and (4) pulmonary and subcutaneous edema. Subcutaneous edema and pulmonary edema are late manifestations of this disorder experimentally, as has been observed clinically. The mechanism in the formation of the fibrinous exudate on the surface of the liver is obscure. If the development of the syndrome had taken place over a sufficiently long period of time, the classic "Zuckergussleber" might have resulted (figs 4 and 5). Together with the observations reported, there occurred general weakness and listlessness, a small and rapid pulse, cyanosis and a decrease in the minute volume output of the heart. It was shown roentgenographically that the heart and pericardium actually decreased in size and assumed a globular shape as the syndrome developed; after the pericardium was resected, the heart assumed its previous size and shape. Not infrequently the compression effect of the tight scar on the heart can be demonstrated fluoroscopically by the limitation of the systolic and diastolic movements of the heart.

The shift of the electrical axis of the heart with a change of position was of slight diagnostic significance in the experiments. Probably owing to the great mobility of the heart and pericardium in the dog

a shift of the electrical axis was found even when the pericardium was markedly scarred. In those experiments in which there was no shift of the axis, the heart was securely immobilized by extrapericardial adhesions. Undoubtedly, the shift of the electrical axis of the heart is of greater diagnostic value in the determination of extrapericardial adhesions, a condition that is different in both its pathologic physiology and its therapy.

In tapping the ventricles for specimens of blood for cardiac output determinations, it was noted that the aspirating needle encountered a definite resistance if the parietal pericardium was thickened and scarred. We hesitate to recommend sticking the pericardium as a diagnostic aid because of the possibility of inflicting an injury to coronary vessels with the needle. In cases in which the diagnosis is obscure, however, may it not be useful as a clinical diagnostic aid?

On the basis of experiment it was found that the venous pressure was the most reliable index to the development of this condition. A rise in venous pressure was always noted before ascites or fluid in the chest could be demonstrated. Further experimentation is being undertaken to determine whether localized pericarditis, as for instance, involvement over only the left ventricle, results in the same sequence of events. A description of localized pericarditis will be reserved for a subsequent publication.

The casing of scar can almost always be resected. Usually a plane of cleavage can be found and separation can be carried out by blunt dissection. This was possible technically in every experiment except one. The exception represents a small percentage of clinical cases in which the scar so intimately involves the coronary vessels and the myocardium that its removal would involve a great hazard.

An important observation brought out in the experimental work was the necessity of excising the scar as completely as possible. Especially necessary was the excision of the scar from the region where the venae cavae enter the heart. At operation the incision in the thoracic wall should be such as to provide exposure of the lateral aspect of the right ventricle and right auricle, as well as of the left side of the heart.

In every experiment in which the pericardial scar was removed successfully a marked improvement in the circulation took place. It was always noted that as the heart was liberated from its encasement of scar an immediate dilatation of the heart occurred. It seemed as though the heart filled better and an immediate improvement in the circulation took place. That the heart returned to its normal shape and size after resection of the pericardium was shown roentgenographically. Following the resection of the scarred pericardium the venous pressure

fell to the normal level. Diuresis took place, and ascites, hydrothorax and edema of the lungs and subcutaneous tissues disappeared. The minute volume output of the heart came back to the normal level. The dog became active and appeared normal in every respect. This improvement almost always seemed to be permanent. In only one experiment did an epicardial scar form after resection of the scarred parietal pericardium and again produce polyserositis. It would have been possible, however, to have resected this epicardial scar after it had formed. The experiments were conducted for several months following pericardiectomy, and as far as could be determined, the operation seemed to be completely curative. The experiments in which the pericardium had been resected did not show any adhesions between the heart and adjacent structures developing subsequently.

#### REPORT OF A CASE

A white boy, aged 14, was admitted to the Lakeside Hospital, on Sept 4, 1929, with pain in the upper part of the abdomen, dyspnea on exertion and weakness.

The parents were of Slovakian stock, both were living. The father had been admitted several times to the psychopathic department of a local hospital, where the diagnosis of manic-depressive psychosis and alcoholism was made. The mother had had exophthalmic goiter and had undergone a partial thyroidectomy in 1925. There was one sister, aged 18 years, who was emotionally unstable but of normal mentality.

The history obtainable from the patient and his family was not accurate. He was born in Cleveland. He had had measles, mumps, pertussis and chickenpox in childhood. Later, he had frequent attacks of sore throat and infection of the upper respiratory tract. A tonsillectomy was performed in 1921 because of these frequent infections. There was no history of acute rheumatic fever, pain in the joints or chorea. At the age of 6, he appeared mentally deficient, and at 11 after several trials at school, he was sent to a state institution for the feeble minded. The intelligence quotients determined by various psychometric test from 1922 to 1927 varied from 55 to 71 per cent. He was at home for two months in the summer of 1928, at that time he became short of breath on exertion and was easily fatigued. There was no history of any febrile illness or ascites at that time. He was then sent to another institution, where he remained until May, 1929. When he returned home he was short of breath and jaundiced and complained of vague epigastric pain with occasional attacks of nausea and vomiting. His cheeks, ears and lips were dusky. His condition improved in the course of a month, but in July, 1929, he came to the Lakeside Hospital Dispensary complaining of shortness of breath. There was no jaundice or fever at that time. In August, according to the history obtained from the mother and sister there was another attack of jaundice with light stools, dark urine, vague pain in the upper part of the abdomen and cyanosis. When he appeared at the dispensary, jaundice was not present.

He was then admitted to the medical ward. He appeared to be fairly well nourished but of obviously low mentality. Moderate orthopnea and cyanosis of the lips and cheeks were present. Throughout the period in the hospital the

temperature was normal. The pulse rate varied from 92 to 120 per minute and the respiratory rate from 24 to 48. The contour of the head was not remarkable, and there were no gross abnormalities of the eyes, ears or nose. There were a few carious teeth, and lymphoid tissue was present in both tonsillar fossae. The external jugular veins were abnormally distended. The thyroid gland was of normal size and consistency. There were no enlarged cervical glands, no tracheal tug and no thrill or bruit in the neck.

The thorax was symmetrical, and its movements were equal on each side. The costal flare appeared to be somewhat restricted, probably on account of the distention of the abdomen. The lungs were clear to percussion and auscultation. The bases were at the ninth rib with excursion of less than one interspace on deep inspiration. No fluid was demonstrable in the pleural cavities. There was no abnormal precordial pulsation or retraction and no Broadbent sign. The

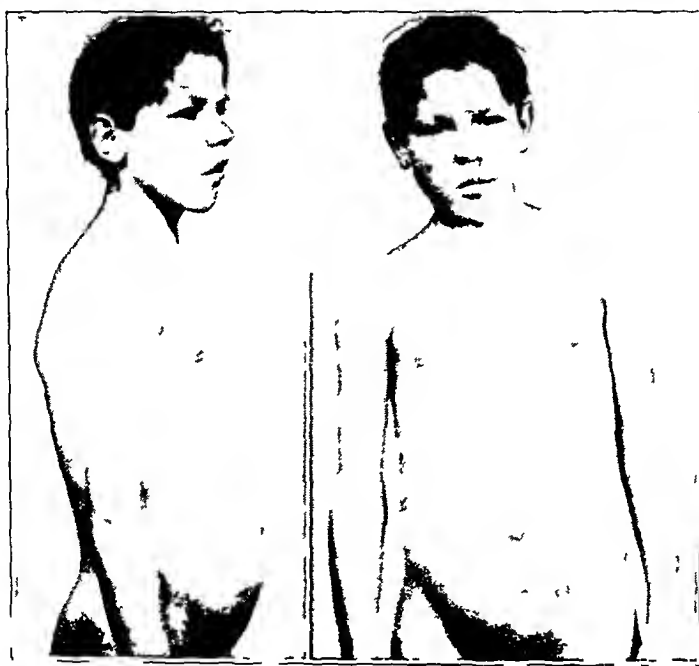


Fig 14—Patient before pericardiectomy

cardiac apex was in the fifth intercostal space at the midclavicular line, the right border of cardiac dullness was beneath the sternum and the upper border was in the third interspace. The cardiac sounds were normal. There was no thrill, friction rub or murmur. A marked pulsus paradoxus was present. The pulse pressure was low, the blood pressure was 106 systolic and 78 diastolic. The abdomen was markedly distended (fig 14). Shifting dullness and a fluid wave could be elicited. The edge of the liver extended to the umbilicus. It was smooth, firm and slightly tender. The spleen was enlarged and firm. The genitalia, reflexes and extremities were normal.

September 13. Stereoscopic films of the chest showed the right apex to be more cloudy than the left and the left lung field to be better illuminated than the right. There was some increase in the hilar markings on both sides, with an increase in the bronchial markings along the right border of the cardiac shadow. There was some thickening of the interlobar septum on the right. The dia-

phragms were fairly smooth and the costophrenic sinuses were clear. The shadow of the heart seemed slightly enlarged. The appearance suggested a slightly thickened pleura over the right side of the chest. The diaphragms appeared of about normal height. There was no evidence of a high diaphragm on either side.

September 20. Fluoroscopic examination of the chest and mediastinum showed the lung fields to be clear and the cardiac shadow slightly enlarged toward the left. The posterior mediastinum was clear, the diaphragms smooth and the costophrenic sinuses clear. There was no definite evidence of mediastinal tumor.

Electrocardiograms were taken with the patient in the dorsal position and also with the patient on the right side. Dr. R. D. Leas reported that the voltage

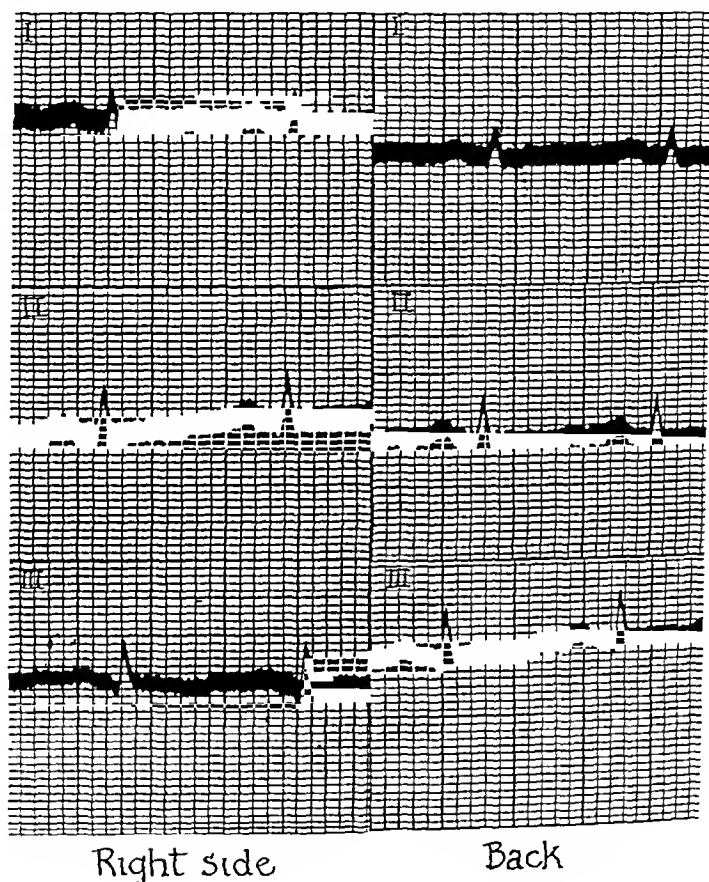


Fig. 15 (September 20) —Low voltage and slurring of Q R S complex with no shift of the electrical axis on change of position.

was below normal and that there was slurring of the Q R S complex in all leads. No shift of the electrical axis was noted with change in position (fig. 15).

The urine was straw-colored and acid, with a specific gravity of 1.014. It did not contain albumin, sugar or cells. A few hyaline casts were found on one examination. The Gmelin test was negative for bile pigments. The Wassermann reaction of the blood was negative. Examination showed red blood cells, 6,680,000, white blood cells, 7,750, hemoglobin, 85 per cent, polymorphonuclear leukocytes, 62.5 per cent, lymphocytes, 27.5 per cent, and mononuclear cells 10 per cent. The icteric index, fragility test of the red blood cells and platelet count were normal. The clotting time was six and one-half minutes and the bleeding time one and one-half minutes.

Abdominal paracentesis yielded 650 cc of clear brownish fluid which did not clot on standing. It had a specific gravity of 1.020 and a cell count of 400 per cubic millimeter.

Except for some reaccumulation of fluid in the abdomen, there was little change in the patient's condition during the period in the hospital. He was kept in bed for several weeks, and was then allowed to be up and about the ward. We saw the patient on the medical ward soon after his admission, and from our experience with adhesive pericarditis in the laboratory we did not hesitate to make the diagnosis of Pick's disease. It was decided, however, to observe the condition over a longer period of time. The patient was therefore discharged from the hospital on October 5.

He was confined to his home. Although he was able to walk about the house, he had no desire to play with other boys. He developed a mild infection of the upper respiratory tract. Dyspnea became more marked. A troublesome cough developed and he was unable to lie recumbent in bed. He was readmitted to the hospital ten days after his discharge.

The patient had orthopnea. An unproductive cough was present. Cyanosis of the cheeks, ears, lips and finger-nails was conspicuous. The veins of the neck, arms and hands were distended. Dilatation of the retinal veins was present. The patient was weak, and he was kept in bed. Edema of the scrotum was present, but elsewhere there was no subcutaneous edema. While he was in the recumbent posture spasms of coughing developed, and he had to be propped up on pillows and a back rest to sleep. The temperature was normal. Pulsus paradoxus was present. The pulse rate varied from 100 to 110 and the respiratory rate from 28 to 40. The systolic blood pressure was from 90 to 100 and the diastolic blood pressure from 70 to 80.

Fluid was never demonstrated in the chest by clinical examination. At times scattered, coarse râles were heard. There was slight impairment of tactile fremitus below the angle of the scapula on each side, but the percussion note was unchanged. There was no precordial activity. The left border of the heart, as determined by percussion, was 10 cm to the left of the midsternal line and the right border of the heart was 3.5 cm to the right of the midsternal line. There was no detectable change in the position of the heart with change in position of the chest.

The abdomen was markedly distended with fluid. The liver was greatly enlarged, firm and slightly tender to pressure, the edge was at the level of the umbilicus. The spleen was large and firm.

October 21. A roentgenographic report by Dr. C. C. McCoy stated: "The film of the heart and the chest in the first oblique position shows evidence of a pleural reaction in the left costo-phrenic sinus which was not noted previously. There might be a small amount of fluid here. There is also a pleural reaction at the right costo-phrenic sinus which seems a little more marked than at the last examination." The measurements of the heart are seen in figure 16.

November 20. Dr. D. Steel made the following report of a fluoroscopic examination: "The cardiac silhouette is triangular in outline. The outlines of the various chambers are obliterated. The amplitude of pulsations is markedly reduced and almost obliterated. The heart is fixed. The respiratory excursion is nil. The retrocardiac space and the retrosternal space are definitely hazy. In the second oblique view the outline of the left ventricle remains posterior to the bi-diaphragmatic angle in all phases of respiration. The superior vena cava and the innominate vein are easily made out. Both hilus regions are definitely increased. Fluoroscopically no tenting of the diaphragms can be made out. The



inner half of the left diaphragm showed practically no motion. The findings suggest an adherent pericardium with changes in the retrosternal and retrocardiac spaces."

The laboratory observations were as follows. The urine contained a slight trace of albumin and an occasional granular cast. Examination of the blood showed white blood cells, 8,000, red blood cells, 6,300,000, and hemoglobin, 105 per cent. The stained smear of the blood showed the cells and platelets to be normal. The percentages obtained in the differential cell count were polymorphonuclear leukocytes, 70, lymphocytes, 20, mononuclears and transitionals, 6, eosinophils, 3, and basophils, 1. The vital capacity did not exceed 1,500 cc., the calculated capacity was 2,700 cc. The venous pressure was determined by inserting an aspirating needle connected to a glass manometer tube containing physio



Fig. 16 (Oct. 21, 1929).—Six foot roentgenogram of the chest.

logic solution of sodium chloride into the median cephalic vein at the anterior level of the heart. The venous pressure measured 350 mm. of physiologic solution of sodium chloride. The normal venous pressure in the median cephalic vein, as quoted by Eyster,<sup>7</sup> is from 40 to 60 mm. of water with an upper limit of 110 mm. A cardiac function test was carried out, which consisted of having the patient walk up and down one flight of stairs four times. This exercise caused marked flushing of the face and shortness of breath. The systolic blood pressure rose from 100 to 130 and the diastolic pressure from 80 to 88. The pulse rate per minute rose from 94 to 120. The blood pressure and the pulse rate returned to their previous levels at the end of thirteen minutes.

*Comment*—A boy, aged 13, presented symptoms of dyspnea on exertion and weakness of about one and one-half years' duration. These were insidious in onset and progressive. Several transient attacks of

jaundice and vague epigastric pain appeared during this period. There was no history of associated fever. There was no history of acute rheumatic fever or chorea. The patient had had frequent attacks of rhinitis and sore throat, and because of the latter the tonsils were removed in 1921. Aside from the mental retardation the patient presented the following symptoms: orthopnea, cyanosis, an increased venous pressure, a low pulse pressure, ascites with enlargement of the liver and spleen, edema of the scrotum, slight pulmonary edema, fixation of the heart and limitation of the diastolic excursion of the ventricles.

The diagnosis of constrictive pericarditis (Pick's disease) was made. The etiology was obscure. The picture presented by this patient was an exact duplication of the experiments in which intrapericardial adhesions were produced by surgical solution of chlorinated soda. The pathologic physiology of the condition was based on the impairment in the filling of the heart produced by a snugly fitting, thickened pericardium. Pericardiectomy was indicated.

*Operation*—The patient was digitalized. The evening before operation, 300 cc of blood was removed and this seemed to relieve some of the engorgement.

Nov 21, 1929. Pericardiectomy was performed. The patient was placed in a semirecumbent position on the operating table and ether vapor anesthesia was administered. The incision was made from the costal margin in the midclavicular line on the left, it curved medially and superiorly to the midsternum, followed the midsternum for 2 inches (5.1 cm) and then curved laterally to the midclavicular line at about the level of the third rib. The pectoralis major muscle was divided at the two lateral arms of the incision. The underlying costal cartilages, sternum and ribs were exposed. The soft structures were separated from the fourth, fifth and sixth costal cartilages and these were divided close to the sternum and at their junctions to the ribs. The mediastinal structures were separated from the sternum by blunt dissection with little difficulty. The sternum was removed by a rongeur over about three fourths of its width and 3 inches (7.6 cm) of its length. The pleural sinus on the left was then dissected from the pericardium. The pleura was adherent to the pericardium, and this separation had to be carried out by sharp dissection (fig 17). During this procedure the pleura was nicked in one or two places, but was promptly closed, protecting the pleural cavity from the entrance of air. The left phrenic nerve was not encountered, presumably it was dissected from the pericardium with the pleura. While the costal cartilages and part of the sternum were being resected, the pulse was irregular. The anesthetist thought that the cyanosis was a little more marked, but no change in the blood pressure or the pulse rate was recorded on the chart that he kept.

The pericardium was then incised over its midanterior portion. It was very thick and the incision was carried deeper and deeper until at one point it actually entered cardiac muscle. The scarred pericardium was incised for about 6 cm (fig 18) and a line of cleavage was found. Separation was carried out with the scalpel. This left a distinct layer of fibrous tissue on the heart, but as the separation proceeded laterally the epicardium seemed to be entirely free from scar. This separation of the pericardium from the heart was carried out laterally over the base and posteriorly by the index finger slowly and cautiously until the

entire surface of the heart was swept clean (fig 19). During this procedure the pulse became irregular at times owing to extrasystoles, though it had seemed more disturbed a little while before, when the costal cartilages were being removed, than it did while the adhesions between the heart and pericardium were actually being separated. The left ventricle was freed before the right ventricle. It was apparent to every one who saw the operation that the heart actually dilated as it was being freed from the adhesions. The anesthetist repeatedly reported that the pulse had become stronger and that the pulse pressure had definitely increased.

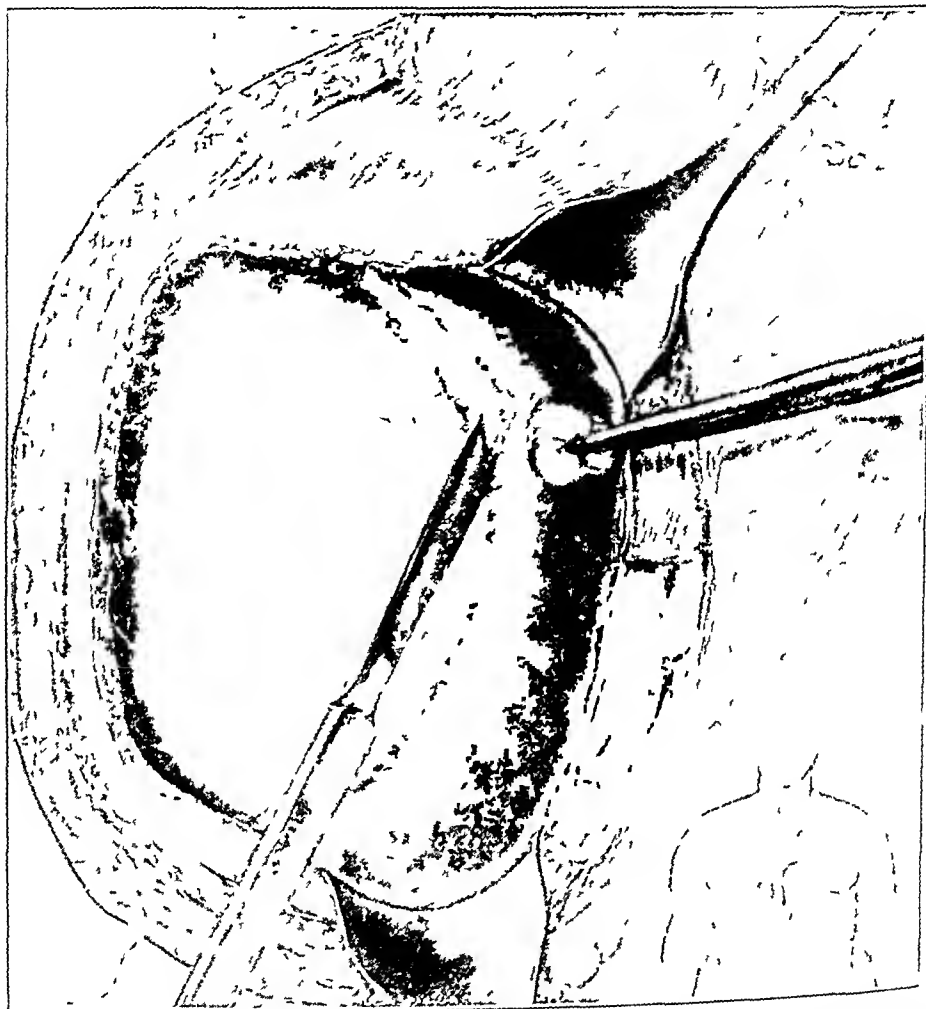


Fig 17—The fourth, fifth and sixth costal cartilages on the left side were resected and the sternum was partially resected. The pleural sinus on the left was dissected from the pericardium.

Lying over the surface of the heart anteriorly was a layer of white fibrous scar about 10 sq cm in area. This was picked up with forceps and removed from the heart with considerable difficulty. Here and there sharp dissection from the ventricle was carried out. After this scar tissue was removed, the anterior coronary vessels could be seen. The surface of the ventricles and the auricle now seemed to be free from scar tissue. The pericardium was 4 or 5 mm thick. It was incised over the base, and the right margin of the pericardium was grasped.

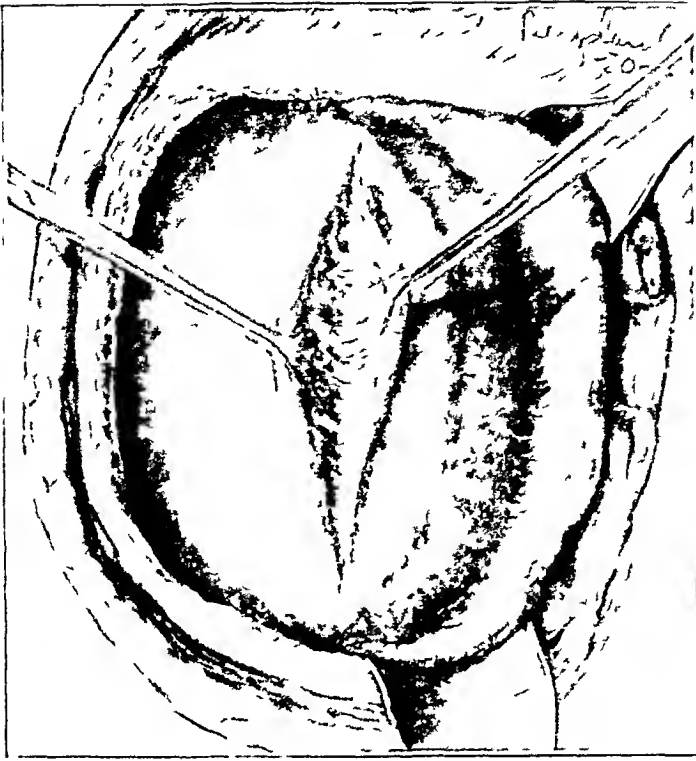


Fig 18—The pericardium was incised over the left ventricle It was difficult to determine the plane of demarcation between scar and myocardium

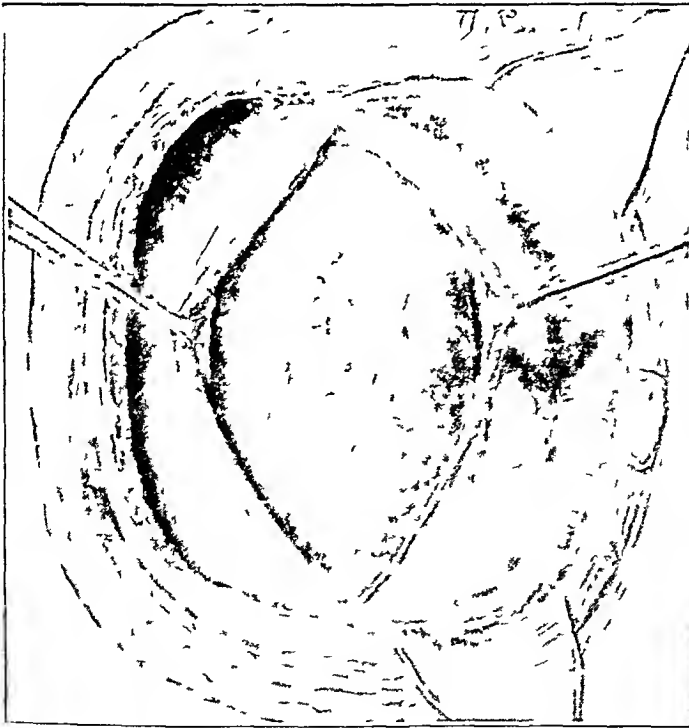


Fig 19—A plane of cleavage was found and separation was carried out by blunt dissection The heart seemed to bulge through the opening in the scar as the separation progressed

with Allis forceps and drawn to the left. This brought into view the right pleural sinus. The latter was dissected from the pericardium well around to the right (fig 20). The exposure of this region, however, was inadequate. The venae cavae could not be seen. Excision was now carried out. The pericardium on the right and over the base of the heart was removed, but excision here was hazardous because we could not see or identify the venae cavae. Excision on the left side was carried well down to the emergence of the pulmonary vessels. The excision of the pericardium was complete except for an area posterior to the heart and a small area over the right auricle where the venae cavae entered the pericardium and where the exposure of the structures was inadequate (fig 21). There was some oozing of blood from the surface of the heart posteriorly, but this was not marked.

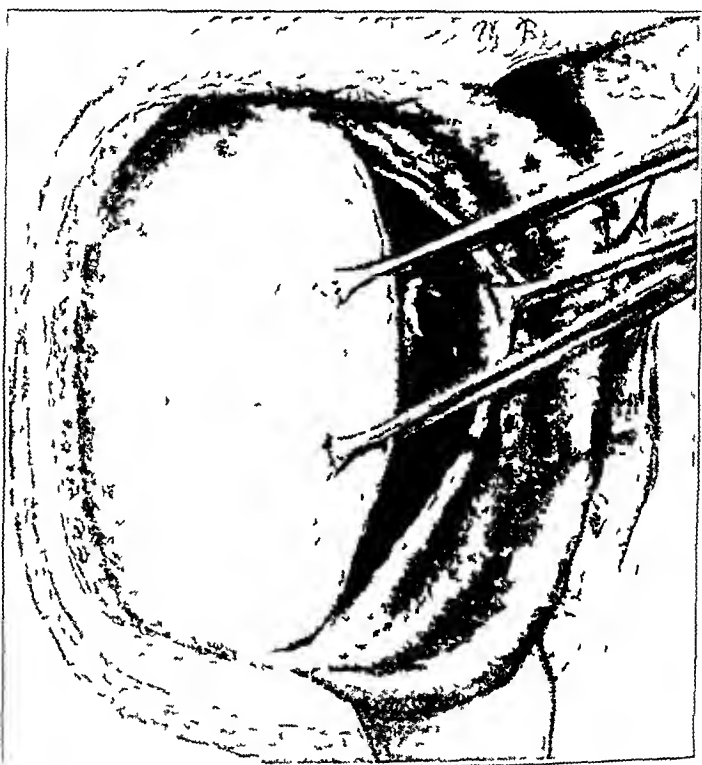


Fig 20—The pericardium over the right side of the heart was drawn to the left. The right pleural sinus was dissected from the pericardium.

The bony framework over the anterior surface of the heart had been almost completely removed by the resection of the cartilages and of part of the sternum. The flap of soft parts was then placed in its bed, the covering of the heart and the pleura on the left being the inner surface of this flap. The soft parts were sutured with two layers of silk and the skin was closed with silk. A small drain was placed in the wound to allow for extravasation of fluid or blood and to prevent cardiac tamponade. The wound was sealed with silver foil and covered with a voluminous dressing.

The excised pericardium is shown in figure 22. Examination by the pathologist yielded the following observations. The fragments of tissue varied in thickness from 1 to 6 mm. One surface of each was granular and well vascularized and the other surface was dense and smooth. The denser surface of

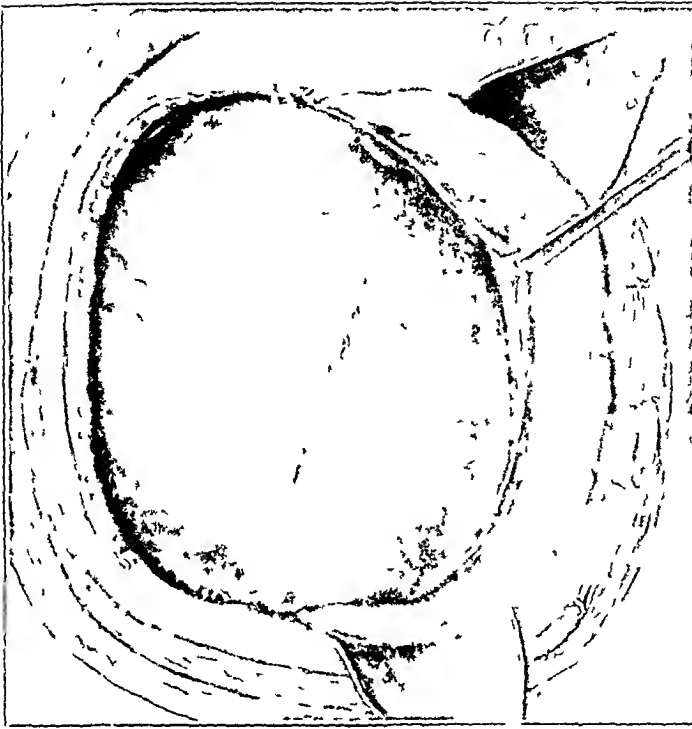


Fig 21—The pericardium was excised as was also a plaque of epicardial scar lying over the left ventricle The coronary vessels stand out well



Fig 22—The portion of the pericardium excised at operation It varied in thickness from 1 to 6 mm Microscopically, this structure closely resembled the scar produced experimentally

one of the specimens contained a small, round, hyaline plaque. Sections through the fragments were essentially similar and showed a dense fibrous tissue which was cicatricial. One side of each section was very dense, the fibers were arranged parallel to one another, for the most part, and there was extensive hyalinization. As the other surface was approached, the tissue became looser and contained many small blood vessels and, in places, lymphocytic infiltration. At the extreme outer edge of some of the fragments there were clusters of fat cells. The hyalinization was not uniform and small hyaline plaques often showed a dense peripheral zone of lymphocytic infiltration. The diagnosis was given as chronic inflammation with hyalinization of fibrous connective tissue.

It was the opinion of every one who observed the patient that the cyanosis of the face and lips was less marked at the end of the operation than before it began, and that the dilatation of the jugular veins was less marked. The blood

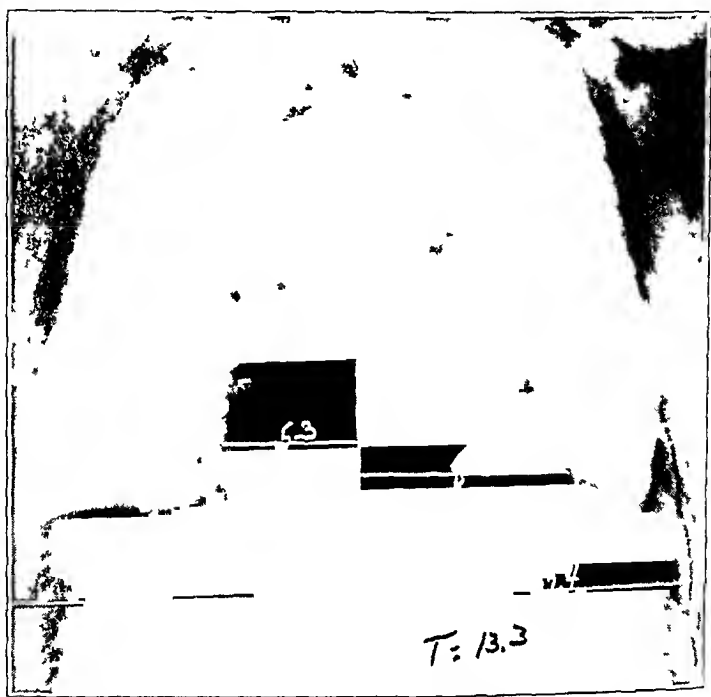


Fig. 23 (Dec. 23, 1929) —Six foot roentgenogram of the chest

pressure was 100 systolic and 56 diastolic. The pulse pressure was doubled by the operation. This meant that the heart was filling better and expelling more blood per beat. The pulse rate per minute was about 140. Within a few minutes after the anesthesia was stopped, the patient regained consciousness. At mid night after the operation, the blood pressure was 114 systolic and 70 diastolic. The cyanosis of the lips had almost completely disappeared. Twenty-four hours after operation the blood pressure was 110 systolic and 70 diastolic and the cyanosis of the lips had completely disappeared. The respiratory rate per minute was about 40, the respiratory movements were shallow, the pulse rate per minute was 120 and the temperature 37.8 C (100 F). Later in the day the temperature rose to 39.5 C (102.9 F), and the patient had a troublesome cough with expectoration of thick tenacious mucus. The respiratory rate per minute at that time was 30, the pulse rate 120 and the blood pressure 100 systolic and 60 diastolic. An occasional small dose of morphia relieved the pain incident to coughing. The temperature diminished in a few days and the cough disappeared.

The drain was removed at the end of twenty-four hours, the bloody serous discharge, which had been profuse at first, quickly diminished. The sutures were removed on the fifth day and the wound was completely closed by the seventh. The patient was allowed out of bed on the fourteenth day. On the eighteenth day the venous pressure was 200 mm of water, the reading having been taken exactly as before. The vital capacity was about 1,150 cc. The blood pressure was 110 systolic and 70 diastolic.

December 23. A roentgenologic report by Dr. D. Steel stated: "Compared to the previous measurements, the transverse diameter of the heart has decreased. This was due, apparently, to a decrease in the left median distance (fig. 23).

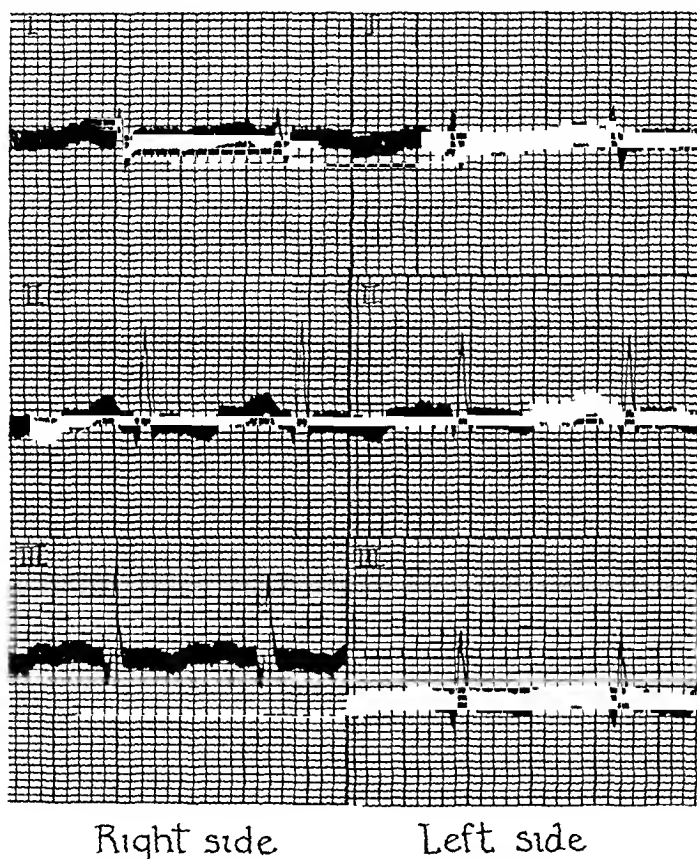


Fig. 24 (December 24) —A slight degree of right ventricular preponderance, with an increase of voltage, less slurring of the Q R S complex and no shift of the electrical axis on change of position.

The median half of the left diaphragm was immobile. As far as can be made out fluoroscopically, the heart does not move upward with respiration. The amplitude of the pulsation has definitely increased since the previous examination."

December 24. An electrocardiographic report by Dr. R. D. Leas stated that the patient had received 12 cc of tincture of digitalis on November 19 and 20, and 8 cc on November 23. There was a slight degree of right ventricular preponderance with an increase of voltage and less slurring of the Q R S complex. There was no evidence of a shift of the electrical axis with change in position (fig. 24).



The patient was discharged from the hospital on December 30. By diuresis he had lost 4 Kg since operation (fig 25). The fluid had completely disappeared from the abdomen. Edema of the scrotum disappeared, as did also the rales in the lungs, the cough and the orthopnea. The patient was up and about the wards without dyspnea, his activities frequently had to be restrained by the nurses. The liver and spleen had not changed in size. At times the slightest trace of cyanosis of the lips was noticeable, at other times cyanosis was absent. The jugular veins were dilated, but the degree of dilatation was considerably less since operation. The venous pressure was 190 mm of water. The blood pressure was 114 systolic and 68 diastolic. The vital capacity was 1,850 cc. The red blood cell count was 5,090,000 and the hemoglobin content 80 per cent. The occasional cast and the trace of albumin found in the urine before operation had disappeared.

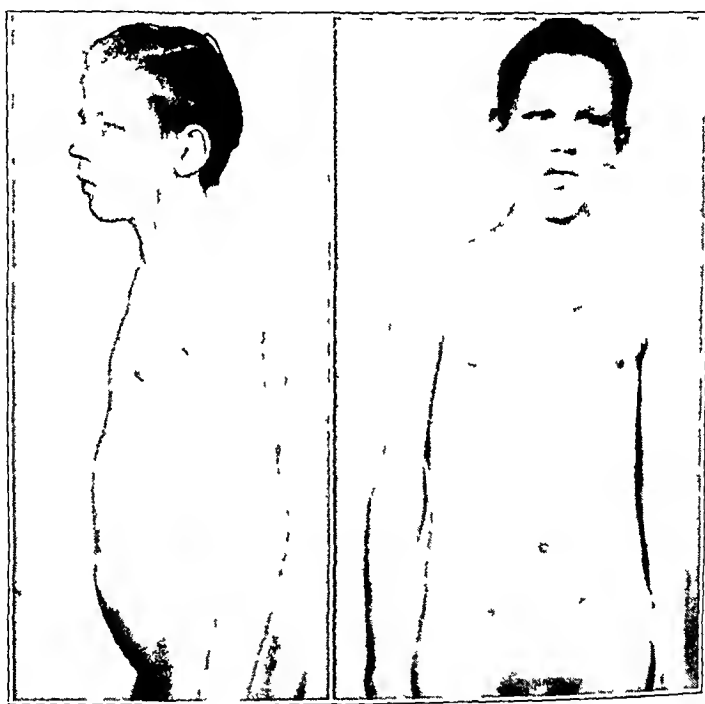


Fig 25—Patient after pericardiectomy

A week later, he could walk upstairs without dyspnea, but he was a little short of breath on running. After climbing the stairs his pulse rate per minute was 104 and his blood pressure 118 systolic and 68 diastolic. The jugular veins were not distended, and there was no cyanosis, cough, edema, ascites or fluid in the chest. The margin of the liver was one fingerbreadth above the umbilicus. There was marked precordial pulsation but no murmur and no pain over the precordium.

Jan 20, 1930. The blood pressure was 118 systolic and 70 diastolic, the venous pressure was 210 mm of water and the vital capacity 2,100 cc. Two weeks later, he could run up a short flight of stairs without dyspnea. The pulse rate per minute was 102, the blood pressure was 124 systolic and 82 diastolic. The venous pressure, taken indirectly by means of the water manometer or Evster, was 170 mm. The edge of the liver was halfway between the costal margin and the umbilicus in the midline. The spleen had decreased in size but was still palpable. The vital capacity was 2,400 cc.

February 20 The patient was very active. The pulse rate per minute was 96, the blood pressure was 122 systolic and 76 diastolic. The veins in the neck were not distended. There was probably the slightest tinge of color to the lips but none to the ears. The vital capacity was 2,300 cc. The liver was still enlarged, but there was no fluid in the abdomen and no edema.

March 19 There was some pulsation in the veins of the neck but no cyanosis. The venous pressure obtained by the direct method, was 17 cm of water. The vital capacity was 2,800 cc. The blood pressure was 120 systolic and 65 diastolic.

March 19 A roentgenogram of the chest showed the heart lying in a more vertical position than before operation (fig 26). The transverse diameter of the heart was less, but this was probably due to the position now occupied by the heart. The diaphragm was smooth and regular and was lower than at the previous examination. The costophrenic sinuses were clear. There was no evi-

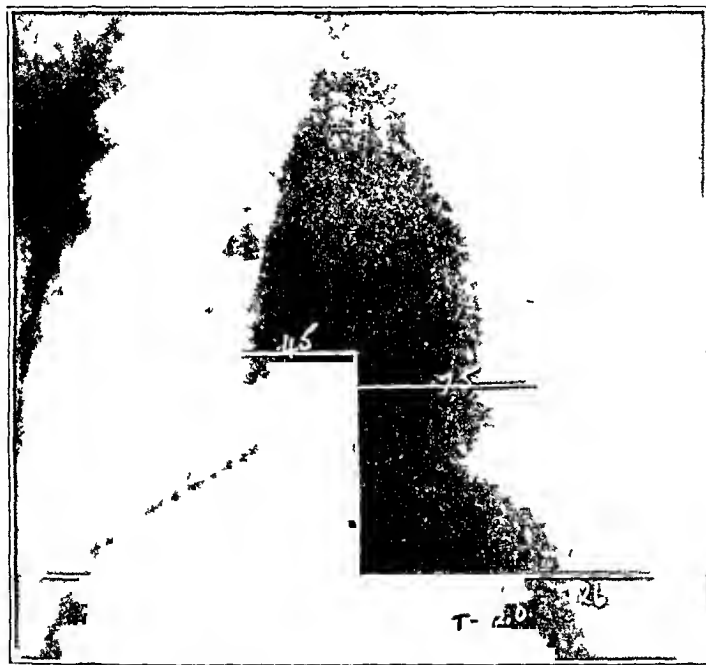


Fig 26 (March 19, 1930) —Six foot roentgenogram of the chest

dence of fluid at the base of either lung. Fluoroscopically, the pulsation of the left ventricle was normal. The pulsation of the right side, however, seemed to be less than normal.

An electrocardiographic report by Dr. Leas showed that the same degree of preponderance of the right ventricle was noted as when the previous records were made. The voltage had increased more than in the previous record. The slurring of Q R S had disappeared, except in lead 1, where it was slight. The progressive increase of voltage and lessening of the slurring first noted in Q R S suggested an improvement in the condition of the myocardium (fig 27).

The sister believed that the patient was brighter and a little more alert mentally. As we recognized that an improvement in the cerebral circulation might bring about this result, further intelligence tests were carried out. The results, however, gave an intelligence quotient of 45. This was less than the result obtained in 1927, but it is altogether probable that at that time the circulatory condition was not impaired.

*Comment*—The diagnosis of adhesive pericarditis (Pick's syndrome) was confirmed at operation. The pericardium was exposed by removal of the left fourth, fifth and sixth costal cartilages and part of the sternum. The pleura was dissected from the pericardium on each side. The pericardium was thickened and everywhere adherent to the heart. The separation of the pericardium from the heart was carried out by sharp dissection over a small area of the ventricles anteriorly, elsewhere the separation was carried out by blunt dissection. The

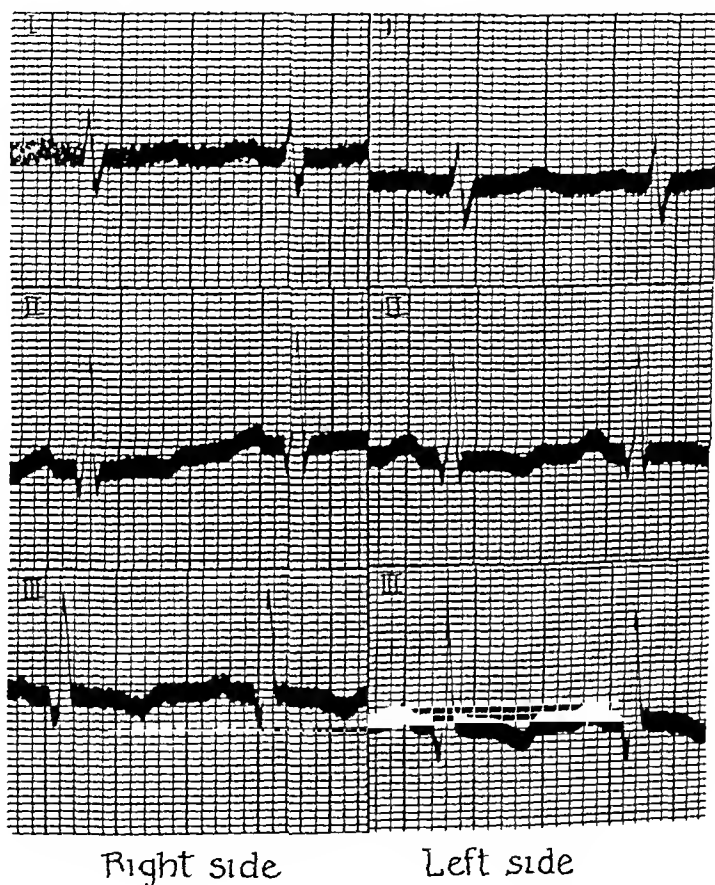


Fig 27 (March 19, 1930)—A slight degree of right ventricular preponderance, further increase of voltage, disappearance of slurring of the Q R S complex except in lead I where it was slight. These observations suggest a progressive improvement in the condition of the myocardium.

exposure of the right side of the heart was inadequate, the venae cavae could not be seen. The pericardium was excised completely except over a small area posteriorly and to the right where the venae cavae entered the pericardium. A small drain was placed in the wound as a precaution against cardiac tamponade, and the wound was sutured.

The improvement was dramatic. As the heart was liberated from its encasement of scar, it definitely dilated, and the anesthetist reported improvement in the condition of the patient. The systolic pressure

rose, and the pulse pressure increased. At the close of the operation the cyanosis of the face, which was conspicuous before operation, had almost completely disappeared. The jugular veins were less distended.

Diuresis subsequently occurred, the patient losing 4 Kg of fluid. The ascites and the edema of the scrotum and lungs completely disappeared. The vital capacity rose from 55 per cent to normal. Orthopnea

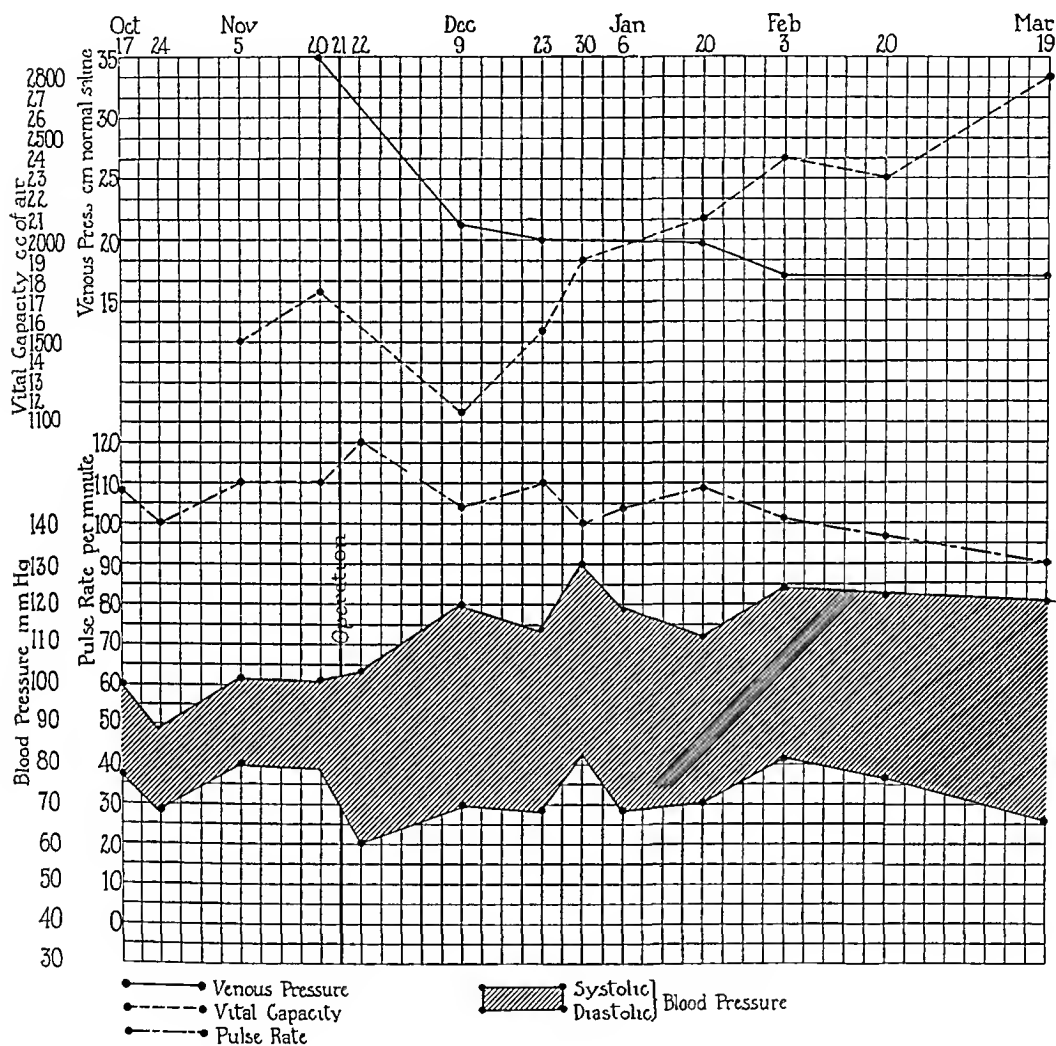


Fig 28—Venous pressure, arterial pressure, pulse rate per minute and vital capacity represented graphically before and after pericardiectomy. The shaded area represents the pulse pressure.

completely disappeared. The systolic pressure rose 15 to 20 mm. The pulse pressure doubled. The venous pressure, as determined by the direct method, fell from 350 mm of physiologic solution of sodium chloride before operation to 170 mm after operation (fig 28).

During the first few months after operation the patient led an active life at home. He could run up one flight of stairs without dyspnea.

but the response to exercise had not fully returned to normal. On Oct 3, 1930 he appeared like a normal boy. His weight was 120 pounds (9 Kg) and his height was 64 inches (162 cm). He was strong and active. He could jump fences, got into numerous fights with playmates of his own age and was able to take care of himself. The blood pressure was normal, but the pulse rate was 110 per minute. The patient, however, was a little excited in contemplation of a venipuncture which was about to be done. The venous pressure was 150 mm, taken in the cephalic vein of the arm. There was no cyanosis. The liver and the spleen were no longer palpable. There was no water in the abdomen or chest.

It will be recalled that the operation did not provide exposure of the right auricle where the venae cavae entered the pericardium. The pericardium was dissected free from this area by blunt dissection, but it could not be excised close to these vessels. The removal of the pericardium over this area, therefore, was incomplete. In view of our experience in experiment 8, we question whether or not the limitation of the movement of the right side of the heart, as seen fluoroscopically, and the slightly increased venous pressure may not have been due to a small segment of pericardium still remaining over this region.

#### BILATERAL EXPOSURE FOR THE RESECTION OF THE PERICARDIUM

As far as could be determined from the literature, the Duval-Barastý incision is the only one that provides an extensive exposure of the heart. Every aspect of the organ can be approached through this exposure. In his operation for the relief of mitral stenosis Cutler had used this incision in six cases, with this experience as a background, he felt that probably this exposure was too shocking to the patient, who was seriously decompensated.

The following is a description of a new incision that seems to be especially applicable to pericardial surgery. It provides a bilateral exposure of the heart without splitting the sternum, without entering the pleural spaces and with a minimal impairment of the respiratory mechanism.

It consists of an H-shaped incision, with the cross-bar of the H extending over the midline of the sternum and the parallel arms of the H placed at the level of the third costal cartilage above and at the junction of the manubrium with the sternum below (fig 29). The transverse incisions extend laterally from the midsternal incision for about 5 cm in each direction. The midline incision is carried to the sternum. The upper transverse incision transects the pectoralis major muscle for a short distance at its origin from the sternum. The two

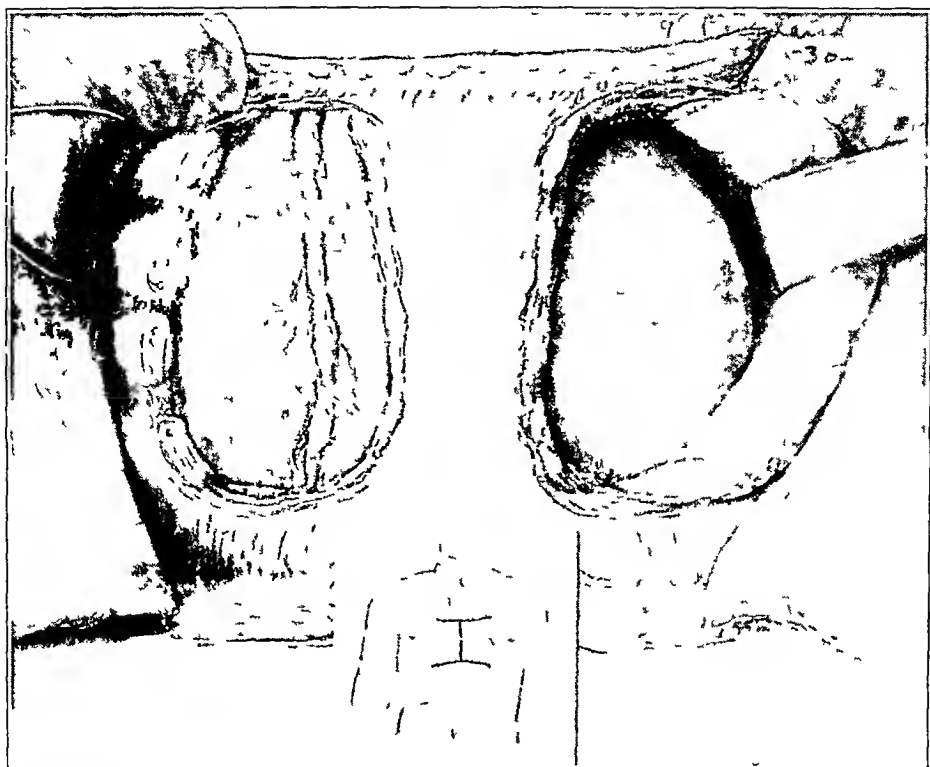


Fig 29—A new exposure for resection of the pericardium. The pleural cavities are not entered. The sternum and the lowest costal cartilages are not disturbed. The mechanics of respiration are thereby little impaired.

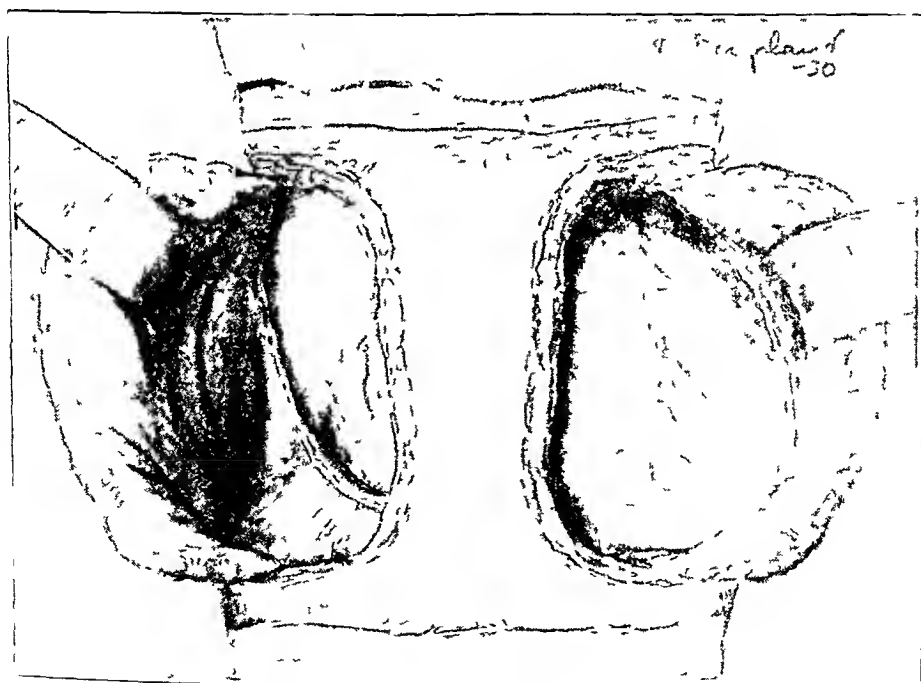


Fig 30—A new exposure for resection of the pericardium. A wide exposure on each side of the heart is provided.

flaps of soft parts thus made are dissected laterally to expose the sternum and the costal cartilages. The third, fourth, fifth and sixth costal cartilages on each side of the sternum are resected. The internal mammary vessels are ligated. The pleural sinus is dissected from the pericardium on each side, and this provides an excellent exposure well around laterally on each side of the pericardium. The left phrenic nerve should be dissected from the pericardium with the mediastinal pleura. The right phrenic nerve may or may not be seen along the superior vena cava. The pulmonary vessels can be seen on each side. An almost complete resection of the pericardium can be carried out, leaving only the portion posterior to the heart (fig. 30).

The sternum is not disturbed. So that the movements of the diaphragm are not impaired the seventh costal cartilage should not be resected. The flaps of soft parts are reapproximated.

We have not as yet used this exposure on a patient. The flaps are so short that we would not anticipate any disturbance to healing, from interference with the blood supply even in the corners of the flaps.

#### COMMENT AND SUMMARY

A form of cardiac decompensation, consisting primarily of scarring and contracture of the parietal pericardium, usually but not always accompanied by intrapericardial adhesions and consisting secondarily of polyserositis, the formation of a fibrinous exudate or scar tissue on the liver and sometimes subcutaneous and pulmonary edema—a syndrome described by Pick and bearing his name—is highly amenable to surgical therapy. Unfortunately surgical measures have had altogether too little application in the treatment for this condition. With few exceptions, internist and surgeon alike are unacquainted with the pathologic physiology underlying the condition and its relief by pericardiectomy.

A method for the production of this disorder experimentally is described. It consists of the application of surgical solution of chlorinated soda in the pericardial cavity. The introduction of this solution results in generalized intrapericardial adhesions, thickening and fibrosis of the parietal pericardium and sometimes of the epicardium, ascites fluid in the chest, enlargement of the liver, together with a fibrinous exudate on the liver, and sometimes pulmonary and subcutaneous edema.

Observations on the experimental production of the Pick syndrome and its relief by pericardiectomy are presented.

Observations on a clinical case of the Pick syndrome and its relief by pericardiectomy are given.

It is hoped that the production of this syndrome in the laboratory will provide further experiences for both internist and surgeon that may have direct application both in the recognition of the condition and in its therapy. To us, these experiments have been highly beneficial. They not only gave us more confidence in making the diagnosis, but they furnished a background of experience that was invaluable for the performance of the operation on the human being.

A new exposure for the resection of the pericardium is presented.

#### ABSTRACT OF DISCUSSION

DR LEO ELOESSER, San Francisco. I should not like to let Dr. Beck's remarkable piece of work go without a word. Last year in an operation on a Chinese child about 4 years of age, I went through a pericardium so extraordinarily thick that I did not know whether I was dealing with pericardium or myocardium until, slowly proceeding, I fortunately found a small, free pericardial cavity. The pericardium was fully half an inch thick, and there were some tender adhesions between it and the myocardium, yet they could be readily separated.

To my disappointment I found, after resecting the pericardium, that it was tuberculous. The child, after making a temporary recovery, died about three or four months afterward of tuberculous meningitis.

DR HOWARD LILIENTHAL, New York. I am always thrilled when I hear a presentation such as we have just had by Dr. Beck. I have wanted cases such as these, but I have had the greatest difficulty in persuading our physicians to turn them over to me. Dr. Groedel of Bad Nauheim happened to be coming to this country at the same time that a patient of his with Pick's disease and calcified pericardium came over. He turned the patient over to me, and I operated on her. She was a woman in the early twenties with enormous ascites, slight hydrothorax on each side, edema of the legs and feet and acutely ill. I believe that I have reported this case before, or, at least, have mentioned it here. My only reason for speaking of it now is that in this patient, whose condition was almost as bad as it could be, I made the Duval-Barastý incision with satisfactory results. If the incision is made almost to the umbilicus, cutting straight through the diaphragm and the center of the sternum with Shoemaker's sternum shears, it is astonishing to see what an enormous exposure of the pericardium will be effected.

Dr. Groedel's patient was relieved by what I did for her and was able to leave the hospital, although I found that the pericardium had literally turned to stone. I did the best I could to get into it from the apex upward, but I found that it was quite impossible, so I made an incision at what seemed to be a less dangerous place toward the base of the heart and opened directly into the auricle. I was naturally alarmed and packed the pericardial wound with gauze. In spite of the complications including a slight infection, the woman was able to be up and around two or three weeks after the operation and left the hospital "improved," even with so little freeing of a comparatively unimportant part of the heart, the auricle. Something caused the improvement of that patient. I cannot believe that it was the splitting of the sternum, because of the calcified pericardium. The roentgenogram had demonstrated that before the operation, but then I thought that the pericardium would be like a nutshell that I could break and peel open as one would an almond from the kernel.



My only reason for inflicting this history on you now is in the hope that Dr Beck will not do the operation which he has cleverly enough devised and which involves cutting the ribs on both sides of the sternum. I believe that the Duval-Barastý incision is not conducive to postoperative shock from what I was able to observe in this one, but very difficult and dangerous, case. I do not believe that this operation would be as dangerous ultimately as to operate on both sides of the sternum, with the danger of entering both pleural cavities, or one at any rate.

I would suggest also that in this operation an anesthetic should be ready for intrapharyngeal hyperpressure.

DR E D CHURCHILL, Boston. I have been impressed by Dr Beck's well rounded presentation of a clinical case supplemented by careful experimental work.

There are many interesting problems presented by an adherent heart. I believe that the adhesions between the two layers of the pericardium are the least important in the production of symptoms. On the basis of one case that came to autopsy I can confirm the experimental observation of Dr Beck that cardiac decompensation can occur without there being any adhesions between the two layers of the pericardium. In the case mentioned the outer layer of the pericardium was drawn laterally and fixed to a scarred area of tuberculosis in the lung. The patient died showing the signs and symptoms of cardiac decompensation with tremendous dilatation and hypertrophy of the heart. Autopsy revealed no valvular disease and no adhesions between the layers of the pericardium.

I think that it must be accepted that the adherent heart is a mechanically disabled one and that this disability need not always be evident clinically. I cannot believe it to be a coincidence that Pick's disease is frequently referred to as "ascites praecox." It seems to be characteristic for the symptoms to occur at this age, the age at which the rapid growth of the body with increasing metabolic needs requires an increased cardiac output. The heart fails to meet this demand because it is unable to increase its diastolic filling, owing to the throttling scar. I have under observation a physician from Nova Scotia who had acute pericarditis in 1897 when he was a student at Johns Hopkins University. He settled in Nova Scotia, carried on the active life of a general practitioner and only recently broke down when, superimposed on his mechanical hindrance, myocardial damage occurred, not only from advancing arteriosclerosis, but from repeated tonsillar infections.

From a study of the case described I have independently come to the same conclusion about the incision that Dr Beck expounds, should my patient come to operation, I should approach the area on the right of the sternum. I cannot agree with the view that the Duval-Barastý incision is without profound effect on the circulation. I used this incision in a case with a diagnosis of pericardial adhesions. The patient died about twelve hours after operation with exactly the same symptoms that Dr Elliot Cutler described in his cases of mitral stenosis. This patient had no pericardial adhesions, and nothing but exploration was attempted. Autopsy showed marked stenosis of the mitral valve.

To repeat the warning of Schmieden, left-sided adhesions should be freed first so that the area of passive congestion is not transferred from the peripheral venous system to the pulmonary bed by release of the right side of the heart first.

DR JOHN ALEXANDER, Ann Arbor, Mich. Within the past year I have operated on two patients with pronounced pectus excavatum because of disabling symptoms. In the first case the sternum had gradually sunken during four years following a slight injury, which was probably not a fracture. On admission there

were dyspnea and much pain, and the heart had been forced into the left hemithorax. At an open operation I lifted the depressed sternum and its attached depressed cartilages and held them in the normal position until bony union had taken place. Nearly a year later, the boy was well and free from the symptoms that required operation.

The second patient was a young woman whose deformity followed a sternal fracture two years before operation. She had severe cardiocirculatory disturbances with disabling anginal pains, which disappeared after operation. Operation consisted in removal of the sternum and portions of its attached cartilages and sewing the pectoral muscles together over the defect. There was direct evidence at operation of firm pressure of the sternum on the heart. In each of these cases the symptoms were probably caused by pressure on the heart rather than by pericardial adhesions.

DR D. B. COLE, Richmond, Va. I rather hesitate to discuss such a brilliant presentation, but wish to report the case of a patient operated on by Dr. Frank S. Johns, who presented symptoms of pressure that were due to pericardial adhesions.

The apex beat of the heart had been pulled to the second interspace anterior axillary line, and the entire heart was rotated upward, backward and to the left. There was also an adhesion from the pericardium to the diaphragm.

The patient first developed signs and symptoms of mitral stenosis followed by those of pulmonic stenosis. His lips became cyanosed, and cardiac decompensation developed. A phrenicectomy was done with considerable relief from symptoms, especially those of decompensation. The patient continued to have signs and symptoms of pulmonic stenosis until large sections of the third, fourth and fifth ribs were removed. This gave the patient an elastic chest wall, and prompt symptomatic relief resulted. The patient has been followed up rather closely and now shows neither signs nor symptoms of cardiac disease.

DR CLAUDE S. BECK, Cleveland. We feel that there should be few mistakes in the diagnosis of the Pick syndrome when it is not complicated by other cardiac abnormalities. It stands out as a fairly distinct entity. The polyserositis, with little or no subcutaneous edema, the increased venous pressure, the absence of disease of the cardiac valves and the limitation of movement of the heart during diastole and systole, when occurring together, give a fairly certain diagnosis. The cases of pericardial adhesions that are complicated by other cardiac disorders, however, are difficult to diagnose. Not only is the diagnosis of this group of cases baffling, but the result following operation for relief from the adhesions cannot be as good as in the former group.

I saw a case in consultation with Dr. Emmett Holt in Baltimore a few weeks ago in which the child evidently had adhesive pericarditis and also defective aortic and mitral valves. There was great decompensation. The heart was very much enlarged. We felt that even though the adherent pericardium were removed the resulting condition would not be sufficiently improved to warrant operation in this case.

Concerning the degree of shock associated with the Duval-Barast exposure of the heart, I can say that in one case in which this exposure was used—the case of a patient with a wound of the heart operated on by Dr. Harvey of New Haven—the operation did not seem to produce shock but certainly in cases of great decompensation it has been our experience that this exposure causes a certain amount of shock.

# ANTEROLATERAL COSTECTOMY FOR INADEQUATE COLLAPSE FOLLOWING POSTERIOR EXTRA- PLEURAL THORACOPLASTY

CARL A HEDBLUM, M D  
CHICAGO

Rest, collapse and compression of the diseased lung are accepted fundamental principles in the treatment for pulmonary tuberculosis. That degree of suspended activity or compression is indicated that is necessary to bring about permanent arrest of the tuberculous lesion, to relax the tension of the scar tissue and to heal cavities. The decreased demands on respiratory function incident to physical inactivity or rest in bed may fulfil the indications. The degree of rest and partial collapse of the lung that results from paralyzing the diaphragm by phrenic crushing or evulsion may turn the tide. The effectiveness of collapse following artificial pneumothorax is due to the relatively complete collapse of the diseased lung. The failures of this method are due chiefly to adhesions preventing complete collapse, to too early abandonment of the method and to complications attributable to it.

The principles underlying posterior extrapleural thoracoplasty are practically identical with those of artificial pneumothorax. The degree of collapse of the lung resulting from it depends on the extent of that of the thoracic wall. It varies within wide limits, but is never as complete as that which follows complete pneumothorax. The results of posterior extrapleural thoracoplasty in properly selected cases are favorable in proportion as the degree of collapse fulfils the indications set by the pathologic anatomy of the lesion. A partial thoracoplasty may be sufficient in case of a strictly localized pathologic process, especially one of the apex of the lung. A limited degree of collapse of the whole thoracic wall may be equally effective in case of a more diffuse involvement, but, generally speaking, the more complete the collapse the more certain it is that the results will be favorable. Sauerbruch writes that an extensive extrapleural thoracoplasty furnishes the best mechanical and anatomic basis for the healing of the tuberculous lesion.

In any individual case the compression of the lung may be said to be adequate, even though partial or submaximal, if the indications for it are fulfilled, but this is difficult to determine beforehand. The failures of thoracoplasty to arrest the tuberculous lesion in properly selected cases are due in large measure to an inadequate degree of pulmonary compression.

The causes of an inadequate collapse following posterior extrapleural thoracoplasty may be inherent in the pathologic process or in the operative procedure

Inflammatory thickening and deformity of the ribs and thickening of the pleura lessens the degree of collapse. A pulmonary cavity surrounded by thick walls of inflammatory tissue, especially if situated centrally, may remain incompletely collapsed. A large chronic tuberculous empyema cavity usually persists in part and always does so if there is open drainage.

The typical posterior extrapleural thoracoplasty consists essentially of resection of the upper eleven ribs flush with their respective transverse processes in two or three stages, at intervals of from one to several weeks. Variations in this operative procedure that most influence the degree of resulting collapse are the length of segments of ribs resected and the time interval between stages.

The longer the segments of ribs removed, under similar conditions, the more complete the mobilization of the thoracic wall and the ultimate pulmonary compression. There is, however, a distinct limit to the degree of mobilization of that thoracic wall that may be induced at any one sitting without the production of paradoxical respiratory movement of the thoracic wall and mediastinal flutter. A similar mediastinal flutter may result from resecting at one stage shorter segments of a larger number of ribs. Generally speaking, the tendency to mediastinal flutter in any given case with a mobile mediastinum is proportional to the area of thoracic wall deprived at any time of its rib support.

Extensive paradoxical movement of the thoracic wall and wide amplitude of mediastinal flutter must be avoided at any cost. This was clearly demonstrated by the pioneer work of Brawner and Friedrich, who lost nearly 30 per cent of their first twenty-seven patients following complete resection of all the ribs in one stage. Any degree of mediastinal flutter always adds to the respiratory load on the other lung and therefore increases the risk of inciting to activity a dormant lesion in it. The only way to avoid it is at a sacrifice of the length or of the number of ribs resected at one stage. The beginning of paradoxical movement of the thoracic wall during the progress of the operation is ample warning.

Perhaps the most frequent cause of an imperfect collapse referable to the operation is regeneration of the ribs between stages. As is well recognized, the major amount of collapse is due to a drop of the whole thoracic wall in the long axis of the body after the thoracoplasty is completed. The longer the interval between the first and last stage the more extensive and advanced the regeneration of the ribs, and the less the ultimate drop of the thoracic wall. But prolongation of the interval between stages may be unavoidable. Frank purulent infection

of the wound, pneumonoma or activity of a tuberculous lesion in the opposite lung, severe hemoptysis or the poor general condition of the patient may necessitate a prolonged interval between stages

A multiple-stage thoracoplasty at prolonged intervals extends the hope of a cure from pulmonary compression to a large group of patients in too poor condition to survive a two-stage or even a three-stage operation, but the resulting compression of the lung from posterior thoracoplasty alone is almost certain to be inadequate because of regeneration of the ribs. The larger the proportion of such otherwise hopeless patients the surgeon accepts for a multiple-stage operation, the greater will be his proportion of cases of inadequate collapse following posterior thoracoplasty

The principle of complete costectomy was embodied in the single-stage operation of Friedrich and Biau already cited. The operation, variously modified, has been described by Brunner, Welles, Jacobaeus and Kay and others, but the secondary complete anterolateral costectomy through a midaxillary incision has not received the attention it merits

#### INDICATIONS

The indications for an anterolateral costectomy, as already suggested, are in part symptomatic and in part anatomic. Persistent symptoms, such as cough with bacilli-laden sputum, hemoptysis and fever or recurrence of such symptoms, following an average degree of collapse, are indications for complete costectomy provided causative lesions elsewhere can be excluded (fig 1). Anatomic indications are persistent pulmonary or pleural cavities. Partial pneumothorax cavities, in my experience, are usually obliterated by an average degree of collapse of the thoracic wall combined with aspiration of the air, but when for any reason this collapse is less extensive a cavity may persist. A chronic empyema usually persists in part even following resection of very long segments of ribs (fig 2). Such a persistent empyema may become secondarily infected or it may perforate into a bronchus, as in one of my patients, drowning him in his own pus. Prolonged absorption may lead to amyloid degeneration and other visceral damage.

Unobliterated pulmonary cavities are usually the source of persistent cough and bacilli-laden sputum and are a potential source of hemoptysis. Such cavities, if centrally situated, require the most complete compression for their obliteration.

A persistent dextrocardia may be in part corrected by the maximal collapse that results from anterolateral costectomy. In one case in my experience, a marked grade of tachycardia was promptly relieved even though the malposition of the heart was corrected only in part.

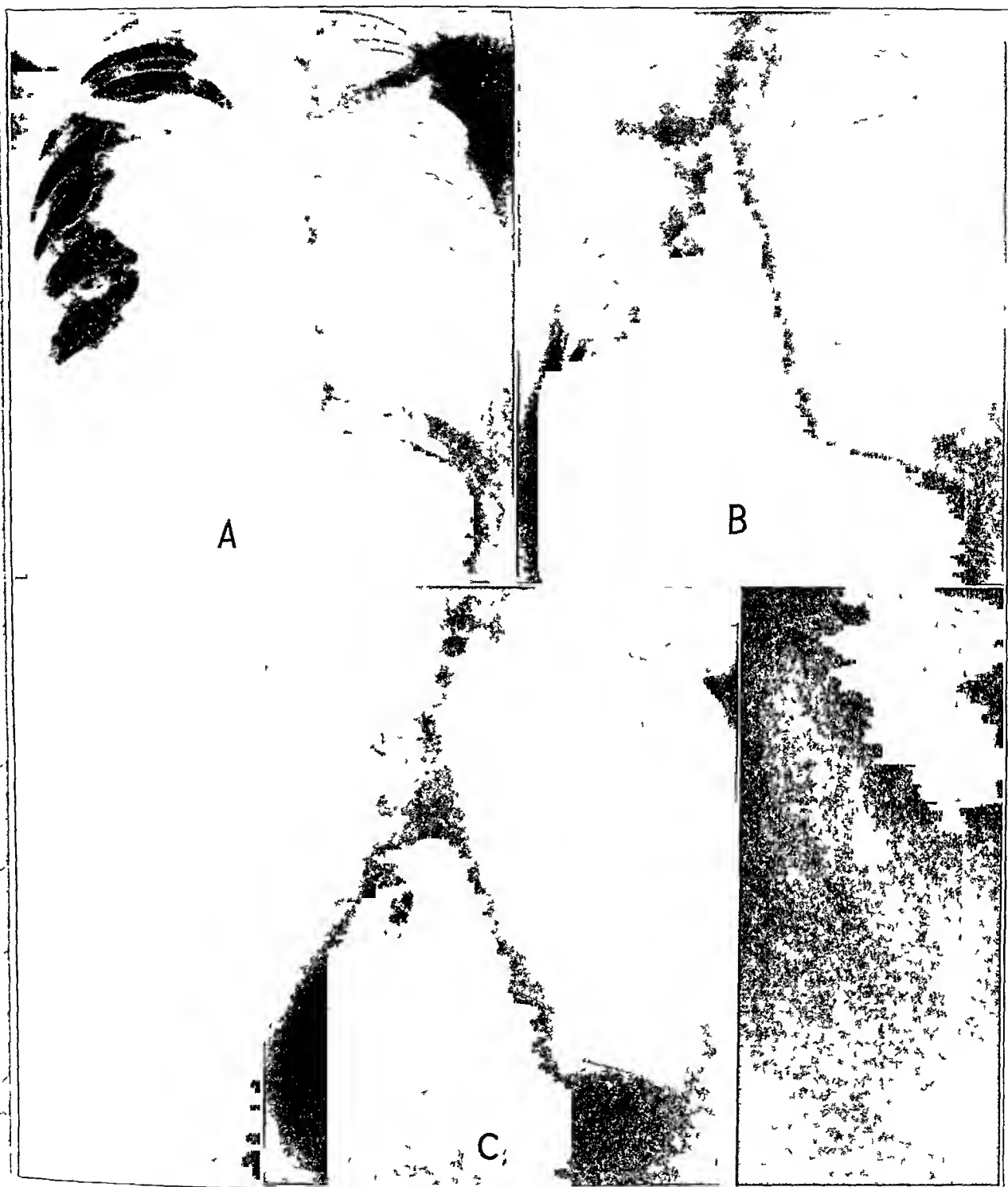


Fig 1—*A* roentgenogram of a woman, aged 26. She had a fever, cough with bacilli-laden sputum, recurrent profuse hemoptysis requiring repeated transfusion of blood, which persisted after incomplete positive pressure pneumothorax collapse. Vomiting, tachycardia and prostration characteristic of profound toxemia occurred *B*, following a three stage posterior extrapleural thoracoplasty at seven day intervals. The hemoptysis ceased, fever subsided and tuberculosis bacilli disappeared from the sputum. There was a marked gain in weight and strength during a period of five months. Following a 'cold' the symptoms recurred and sputum became positive *C*, after a two stage anterolateral costectomy at a fourteen day interval. The patient again became relatively symptom-free and has remained so during the year that has elapsed since the last operation.

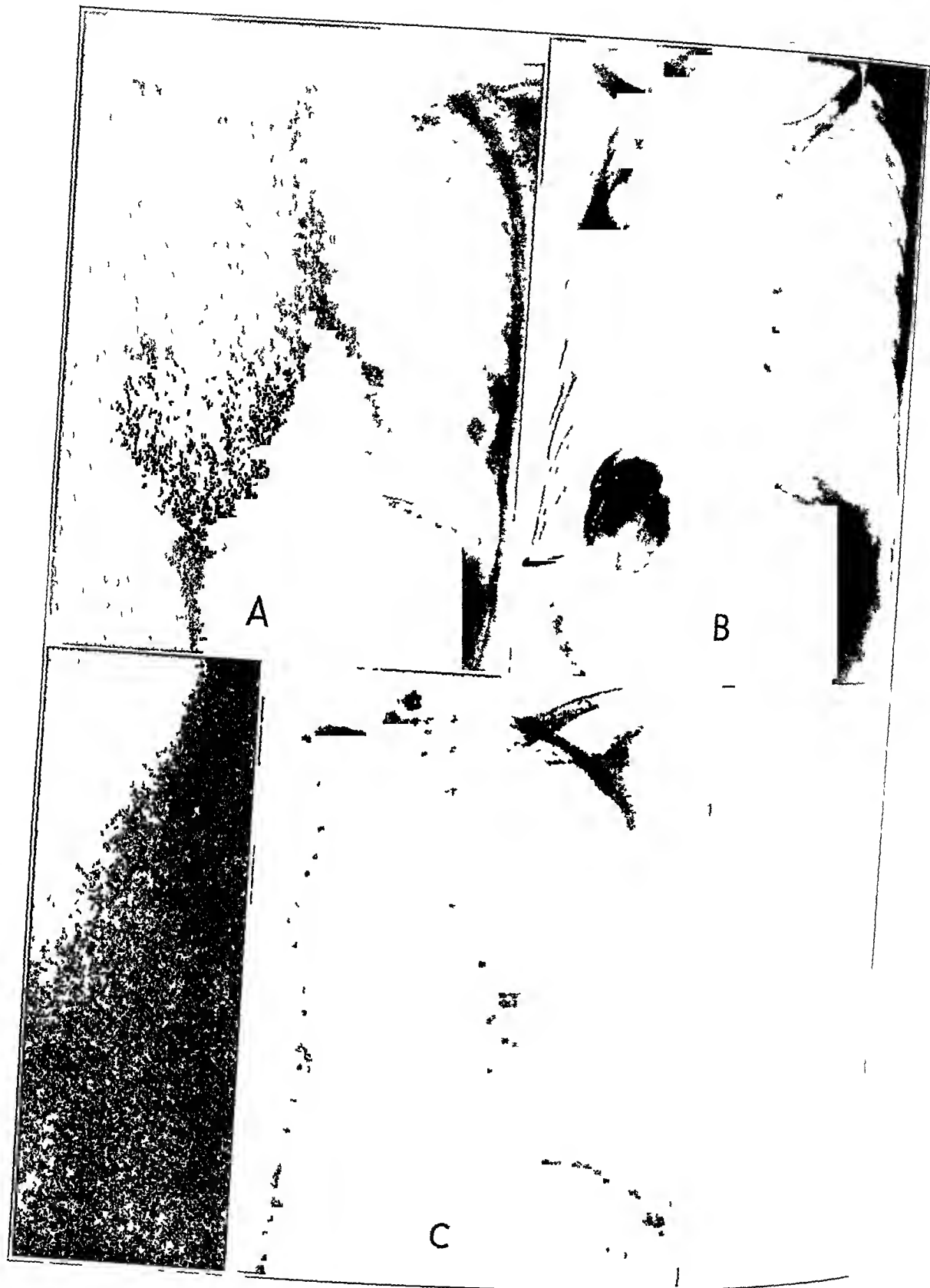


Fig 2—*A*, roentgenogram of a woman, aged 30, who had secondarily infected tuberculous empyema developing two months after artificial pneumothorax therapy was begun. *B* after posterior extrapleural thoracoplasty. The residual cavity is shown filled with a sodium bromide solution. *C*, showing cavity completely obliterated following a two stage anterolateral costectomy. Residual sinus shown in roentgenogram is closed completely. Marked general improvement has persisted during the year and a half elapsing since operation.

## TECHNIC

Anterolateral costectomy is technically not difficult. If the nerve trunk was crushed at the time of the posterior resection, costectomy can be done with a minimum of local anesthesia. A little gas anesthesia may be indicated only to relieve psychic stress. The incision is made in the midaxillary line (fig 3). The muscles of the anterior and posterior axillary folds are undermined and thus not damaged (fig 4). Usually it is desirable to remove the upper nine or ten anterolateral segments. This can be safely accomplished in two stages, the upper five being resected first. For the approach to the first rib, the position of the



Fig 3—Showing midaxillary incision for anterolateral costectomy

patient is important. He lies on his side with the arm on the side to be operated on, extended above his head, where it is tied to a support. The incision extends in the axilla to the second rib. The soft tissues are next undermined, exposing the ribs.

The secret of the relative ease with which the ribs may be resected in spite of a limited exposure lies in the fact that their posterior ends are already partly mobilized and serve as a pivot on which the rib may be rotated in separating the periosteum. The rib is first liberated from the periosteum in its median, most accessible portion (fig 5). It is then retracted outward, which facilitates separating the periosteum to the costochondral junction where it is cut. The mobilized anterior extremity of the rib can then be pulled forward which facilitates the separation



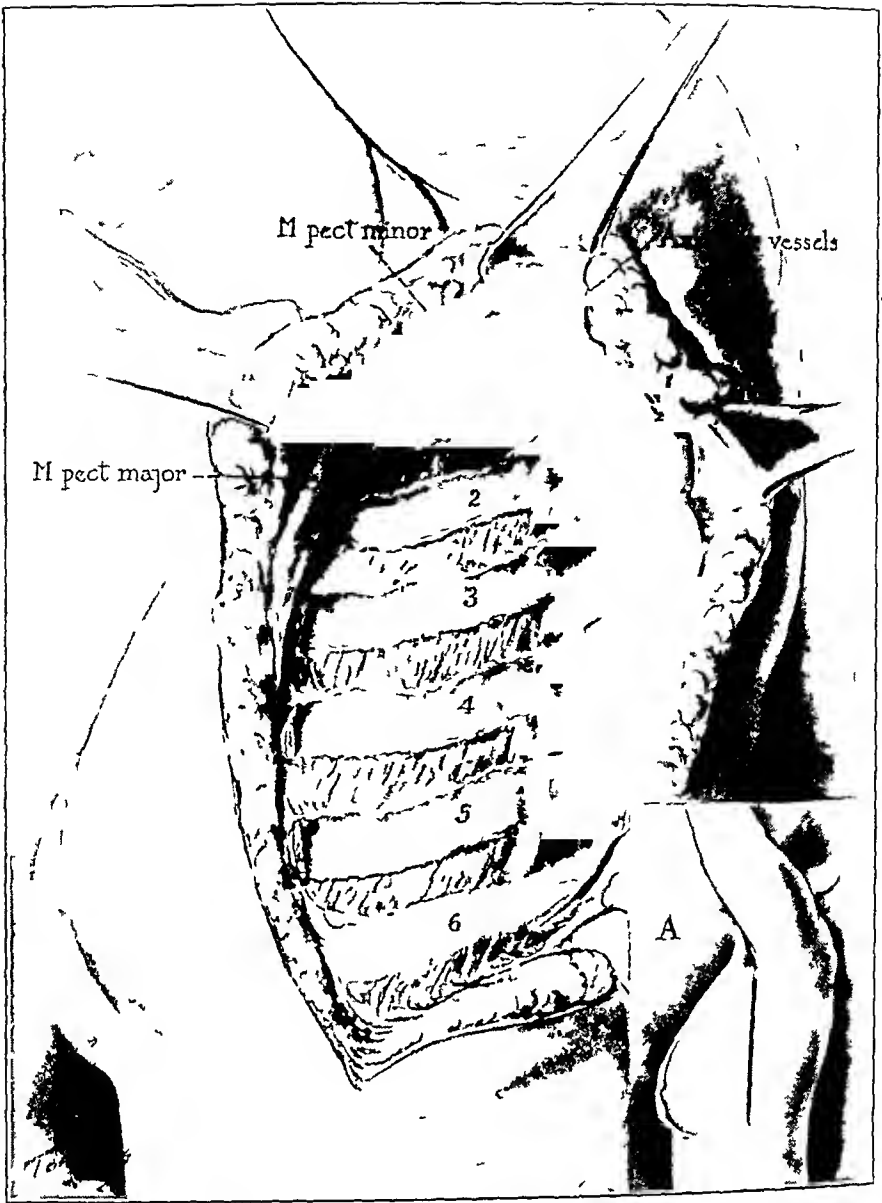


Fig 4—Exposure for resecting the anterolateral segments following posterior extrapleural thoracoplasty Note good access to first rib

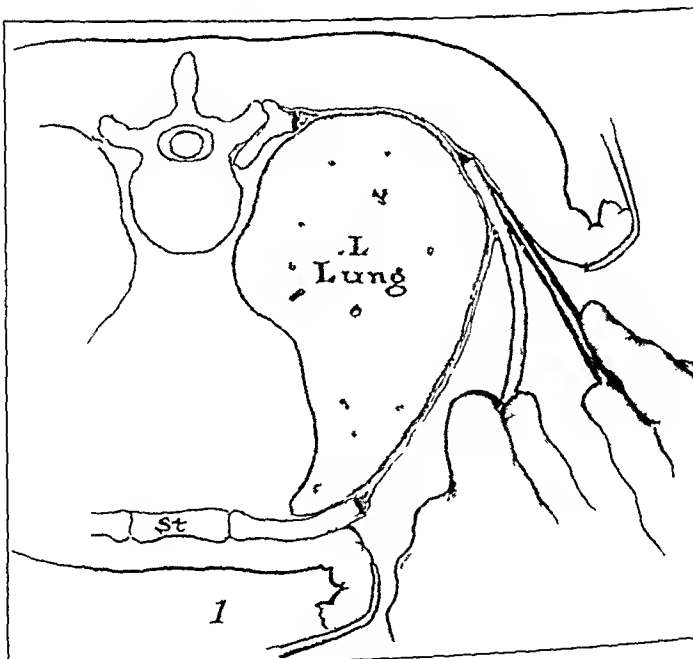


Fig 5—Technic for separating the periosteum from the portion of the rib lying under the muscles posteriorly and under the scapula

of the periosteum posteriorly. This is done first on its outer aspect, then from its upper edge. The rib is now lifted for the stripping of the periosteum from its lower edge and inner aspect. This technic reduces trauma to the intercostal vessels and consequent bleeding to a minimum. Rotation in a large arc now serves to liberate the posterior extremity. If sufficient time has elapsed between the posterior and the anterolateral resection, a spur often forms at the proximal end of the anterolateral

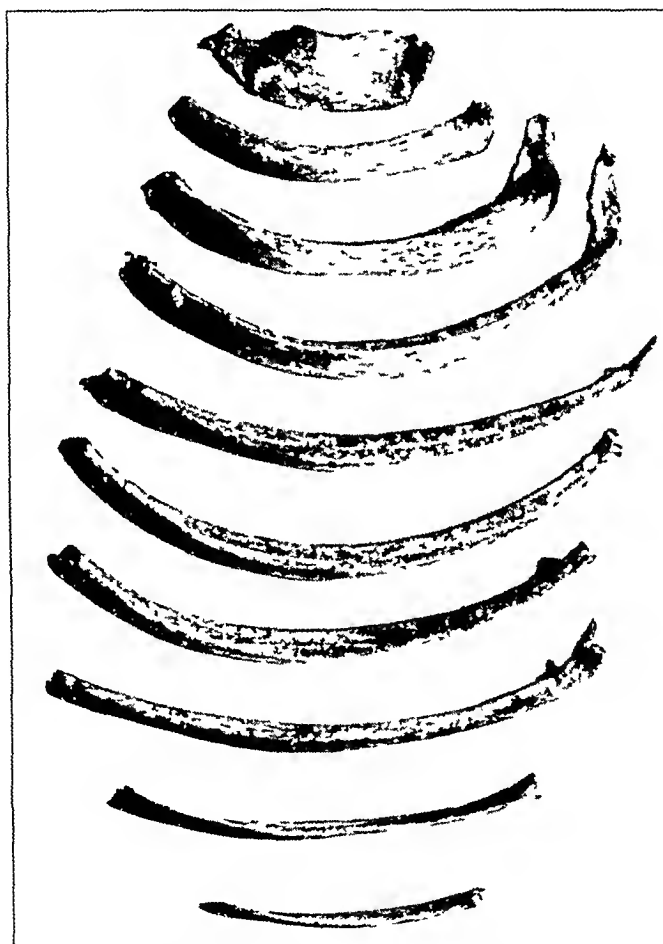


Fig 6—Anterolateral segments of upper ten ribs to costochondral junction, total length 157 cm. Note hooklike projection of the proximal end of third and fourth ribs.

segment to be resected. Owing to the drop in the rib following the first resection, this spur always points upward (fig 6). When the rib is rotated on its long axis for the purpose of liberating this portion, it should be in the direction that lifts this angling spur away from the pleura. If rotated in the opposite direction, it may penetrate the lung and cause infection of the wound and a bronchial fistula. This occurred in one of my cases. Only rarely, in my experience is union to the regenerated posterior segment so firm as to require resection. If necessary,

this can be accomplished under the guidance of the finger with an angled rib-resecting instrument

Especial care is necessary in liberating the first rib, but if precaution is taken to keep inside the periosteal sheath, the overlying subclavian vessels will not be injured

The fascia and skin are closed in layers with a buried Penrose drain, from which a strand of catgut extends through the lower edge of the incision. This drain is removed in twenty-four hours

At the second stage, the incision is prolonged downward to the eleventh interspace. The lower ribs can be satisfactorily exposed through this incision. The technic for their removal is identical with that for resecting the upper ribs

### RESULTS

During the last four years I have performed this secondary anterolateral costectomy in twenty-six cases. The indications were persistent symptoms after the posterior thoracoplasty in eight cases, recurrence of symptoms after a symptom-free period of four months in one, and of ten months in another. There was an average grade of collapse of the thoracic wall from the posterior resection in all these cases. In three, regeneration of the ribs in the course of a multiple-stage operation prevented a satisfactory anatomic degree of collapse, and in all, symptoms persisted. In two, there were large unobliterated pulmonary cavities and persistent pneumothorax cavities. In eleven, there were unobliterated empyema cavities secondary to active pulmonary tuberculosis. The parietal pleura overlying a residual cavity was resected later in all of these cases, with complete healing.

In all these cases the anterolateral resection was as well or better tolerated than the posterior resection. There was one death attributable to the operation. This patient showed no more immediate reaction than the average. He ate his supper the evening of the day of operation. Gradually symptoms of an acute infection developed, and he died on the ninth day. Blood culture showed a hemolytic streptococcus. One patient had a persistent hemoptysis for which a secondary pneumolysis was performed, using the pectoral muscles to compress further the upper lobe of the lung. The hemorrhages were almost completely checked for a period of twenty-four months, but she died thirty-six months after the anterolateral costectomy, from a profuse hemorrhage. A bronchoscopic examination had been attempted on this patient at the Chevalier Jackson Clinic previous to the operation, but failed because of the profuse bleeding. One patient had a persistent mild grade of paradoxical movement of the thoracic wall, with moderate dyspnea on exertion. The lower five ribs had been resected elsewhere about a year before. The regenerated segments were removed at the posterior

operation and did not regenerate a second time, leaving the lower part of the thoracic wall permanently mobilized. In all the other cases regeneration of the ribs has occurred.

The sputum of all of these patients remained free from tuberculosis bacilli. One patient had symptoms of a mild involvement of the other lung during the first year following the operation, but these symptoms subsided. The empyema cavity in all cases is healed. Sixteen of the twenty-six patients are symptom-free, except for more or less dyspnea on exertion. One of these patients is doing heavy farm work. Eight may be classified as greatly improved, the persistent symptoms being varying grades of weakness, dyspnea on exertion and tachycardia. One has a persistent and one, recurrent attacks of unproductive cough.

There is no loss of function of arm and shoulder except some limitation in extension of the arm, in a few cases, due to the contracting scar. There is no more noticeable deformity when the patient is dressed than results from the posterior thoracoplasty. The degree of collapse of the thoracic wall and pulmonary compression is maximal in all cases.

#### SUMMARY

Pulmonary collapse or compression offers the best if not the only hope of a cure to patients with pulmonary tuberculosis who do not get well under modern sanatorium treatment or its equivalent.

The effectiveness of artificial pneumothorax is due chiefly to the resulting relatively complete collapse of the lung.

Posterior extrapleural thoracoplasty is identical in principle with pneumothorax.

The degree of pulmonary compression following posterior extrapleural thoracoplasty varies within wide limits, but is never as great as following complete pneumothorax. A large proportion of incomplete cures and recurrences are due to a degree of compression inadequate to the individual case.

Compression following posterior extrapleural thoracoplasty may be considered inadequate if symptoms referable to the partially collapsed lung persist or recur, or if there remain unobliterated pleural or pulmonary cavities.

The cause of an inadequate collapse may be inflammatory stiffening of the lung or thoracic wall, or regeneration of the ribs between the stages of the operation.

Anterolateral costectomy following posterior thoracoplasty consists in the subperiosteal resection of the remaining rib segments.

The indications for anterolateral costectomy are persistent or recurrent symptoms referable to the incompletely collapsed lung or to the unobliterated pulmonary or pleural cavities.

This operation results in a maximal pulmonary compression and obliterates pulmonary and pleural cavities or reduces them to a minimum size. It also facilitates pneumolysis when indicated for a persistent pulmonary cavity and is a necessary preliminary to resection of the pleura over residual empyema cavities.

The operation is technically not difficult, is relatively well tolerated and the postoperative discomfort is minimal.

By making possible an adequate degree of collapse in multiple stages at relatively long intervals, it extends the indication for pulmonary compression to a considerable group of patients in too poor condition for a two-stage or three-stage operation.

Anterolateral costectomy is the logical procedure for "following through" in cases in which for any reason compression following posterior thoracoplasty is inadequate.

In my series of twenty-six cases of anterolateral costectomy, there has been one operative death from sepsis and one subsequent death from hemorrhage. A maximal degree of pulmonary compression and obliteration of cavities was effected in all cases.

# THE UNFAVORABLE RESULTS OF PHRENICECTOMY \*

FRANK B BERRY, M D

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During the past decade, a rather extensive literature has accumulated on the surgery of the phrenic nerve as applied to pulmonary tuberculosis, bronchiectasis and abscess of the lungs. This literature has become increasingly voluminous, particularly in the last four or five years. Most of the authors have dealt with the subject (1) purely from the academic standpoint, (2) by reporting series of cases varying in number from 1 to 600, or (3) by combining both of the foregoing methods of approach. The technic of phrenicectomy and exeresis has been adequately described many times, and as a result the procedure, with minor individual variations, has become standardized. The accidents to be avoided and cautions against them have almost all been directed toward errors in technic and how to avoid them, and also to the possibility of grave and unavoidable mediastinal hemorrhage.

Among the technical errors that have occurred, even with experienced operators, are injury to the thoracic duct, the vagus or the sympathetic nerves, the brachial plexus, the adjacent great vessels or important branches of them and the dome of the pleura. These and the anomalies or abnormal positions of the phrenic nerve itself have already been detailed at length so often and so well that I need waste no time on them. Furthermore, they should always be to the fore in the mind of any surgeon while performing operations in this region.

I shall not discuss the indications for phrenicectomy whether the nerve should be crushed, divided, resected or avulsed, nor the results obtained from these various procedures. I have attempted no analysis of my 160 cases quoted herein, which comprise operations of all the aforementioned types by Drs Lambert, Greenough, Weeks and myself in various institutions during the past five years. This study has been strictly limited to a small group of cases in which there have been unfavorable reactions immediately following operation on the phrenic nerve that has resulted in paralysis of that portion of the diaphragm supplied by it. In all of these instances the operative procedure has been perfectly performed without technical slip of any sort. Except for the possibility of mediastinal hemorrhage, this phase of the subject has scarcely been mentioned in the literature of any of the English speaking

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\* From the Department of Surgery, College of Physicians and Surgeons, New York, and the First Surgical Division, Bellevue Hospital.

countries, doubtless for the reason that the chances for poor results directly attributable to the operation have been considered to be negligible. The operation is usually presented to the patient as one without risk, which the surgeon hopes will prove of great benefit, but which in all events can do no harm. That accidents and complications can and do occur, however, in no way referable to the operative technic, has been recognized especially by the Germans, and numerous cases of such sequelae have been reported by them, a few have also been reported by the French and Italians. In some of these the outcome was fatal, in some the patients recovered.

From a review of the literature of the past five years I have obtained a total of 4,697 cases of phrenicectomy, including crushing and simple division of the nerve. Of these, 3,050 were reported by Germans and Austrians, 1,217 by Americans, English and Canadians, including my series, and 430 by French and Italians. The individual series recorded by these authors consisted of from 1 to more than 600 cases. In this entire group of 4,697 cases there have been 57 (1.2 per cent) complications directly attributable to the operation, and of these, 26 (0.5 per cent) were fatal. It thus becomes clear that when these sequelae occur they are of a most serious nature, as over 40 per cent of them have ended in death.

#### HEMORRHAGE

As the phrenic nerve and its accessories, in part of their course, lie in intimate contact with the subclavian, jugular and innominate veins, and the subclavian, internal mammary and pericardiophrenic arteries, hemorrhages that occur are ascribed to trauma to one of these vessels by the avulsion of the nerve. Most commonly they seem to be due to a tear of the pericardiophrenic artery, although injuries to the large veins have also been mentioned. Two instances of fatal hemorrhage have been reported by Kleinschmidt<sup>1</sup> as having occurred in Sauerbruch's clinic; another by Rist, one by Thomopoulos<sup>2</sup> and two by Herben,<sup>3</sup> six in all. Likewise, Matson<sup>4</sup> mentioned a case of nonfatal hemorrhage due to pulling away a bit of the wall of the jugular vein. It is easy to understand how this danger would probably be greatest with those patients in whom fibrous mediastinitis is present with marked scarring and retraction. Fortunately, I have not as yet met with this terrifying catastrophe. Furthermore, whenever the nerve cannot be readily drawn up from the mediastinum or when a chronic mediastinitis is recognized or suspected

1 Kleinschmidt, P. *Deutsche med. Wchnschr.* **53** 473, 1927.

2 Thomopoulos, A. *Paris* 1925.

3 Herben, G. F. *Personal communication to the author.*

4 Matson, R. C. *Tr. Coll. Physicians* **49** 167, 1927.

I am always satisfied with a moderate resection of the nerve such as may be obtained without undue traction

Matson, in his excellent article, described the presence of a small bit of anthracotic lymph gland that accompanied an avulsed nerve in one instance, and mentioned this as an etiology for a possible suppurative mediastinitis. No such cases have been reported up to the present, however. Of a somewhat similar nature, but due to a tear of the mediastinal walls, are two cases reported by Deist<sup>5</sup> and another by Sergent, Baumgartner and Bordet<sup>6</sup>. In Deist's patient a pneumothorax developed, and later a pyopneumothorax, following avulsion of the nerve, in Sergent's case exsufflation of the nerve caused pneumothorax and mediastinal emphysema. Both of these patients died.

Other causes of death have been given as follows. Berg<sup>7</sup> described death six hours after operation from pulmonary embolism as shown at autopsy. Chandler<sup>8</sup> ascribed death in his patient four hours after operation to pulmonary edema. Curti's<sup>9</sup> patient died in ten days with persistent dyspnea and tachycardia. Hedblom<sup>10</sup> reported one death from respiratory insufficiency. Leiche's patient with bronchiectasis mentioned by Sergent and his collaborators, died on the operating table of asphyxia shortly after the nerve had been avulsed. Necropsy showed the opposite lung flooded with the secretions, hence the patient, dyspneic and with his ability to cough diminished, had literally drowned in his own secretions. The remaining thirteen deaths in this group of fatalities, including the case to be cited, were due to pneumonia or a spread of the tuberculous process in either or both lungs immediately subsequent to operation (table).

Thirty-one patients, although they survived, were made distinctly worse by the operative procedure, which seemed to produce either a prompt spread of the disease or the development of pneumonia in one or both lungs. There is one exception, the case of a patient with tuberculosis and positive sputum, reported by Loewenthal<sup>11</sup>. Following phrenicectomy, a typical abscess with cavity formation, fluid level and characteristic abscess sputum appeared in the lung of the side on which operation had been performed and then gradually cleared up spontaneously.

5 Deist, H. Beitr. z. Klin. d. Tuberk. **63** 424, 1926

6 Sergent, E., Baumgartner, R., and Bordet, F. Bull. et mem. Soc. med. d. hop. de Paris **50** 20, 1926

7 Berg, W. Deutsche med. Wchnschr. **54** 874, 1928

8 Chandler, F. G. Brit. M. J. **2** 605, 1928

9 Curti, E. Policlinico (sez. prat.) **34** 1474, 1927

10 Hedblom, C. A. J. Michigan M. Soc. **28** 535, 1929

11 Loewenthal, M. Beitr. z. Klin. d. Tuberk. **71** 712, 1929



## REPORT OF CASES

CASE 1—M K, a woman, aged 35, single, was admitted to Summit Park Sanatorium in December, 1926. There was extensive tuberculosis of the right lung with fibrosis and cavitation and with considerable retraction of the heart and trachea to the right. The left lung contained a healed lesion at the apex. Sputum was positive. She improved very slowly while at the sanatorium, and it was finally thought that phrenicectomy might be beneficial. This was performed on Nov. 21, 1928, and was followed by considerable gastric disturbance. Fluoroscopic

*Causes of Death Following Phrenicectomy*

Author	No of Cases	Cause of Death	Time
Berg, W. <i>Deutsche med. Wchnschr.</i> 74: 871, 1928	1	Pulmonary embolism	6 hours
Chandler, I. G. <i>Brit. M. J.</i> 2: 605, 1928	1	Pulmonary edema	4 hours
Curti, E. <i>Polichinico (ser. prat.)</i> 34: 1174, 1927	1	Dyspnea and tachycardia	10 days
Dumarest and Bernard. <i>Rev. de la tuberc.</i> 9: 161, 1928	2	Contralateral spread of tuberculosis	?
Deist, H. <i>Beitr. z. klin. d. Tuberk.</i> 63: 424, 1926	2	Pneumonia, pyopneumothorax	?
Hedblom, C. A. <i>J. Michigan M. Soc.</i> 28: 535, 1929	1	Respiratory insufficiency	?
Kleinschmidt, P. <i>Deutsche med. Wchnschr.</i> 53: 473, 1925	2	Hemorrhage caused by avulsion of nerve	?
Morone, G. <i>Ann. ital. di chir.</i> 4: 189, 1925	1	Pneumonia	9 days
Schnippenkotter, W. <i>Beitr. z. klin. d. Tuberk.</i> 65: 56, 1927	1	Spread of tuberculosis	?
Schurich, A. <i>Beitr. z. klin. d. Tuberk.</i> 61: 552, 1925	1	Contralateral spread of tuberculosis	?
Sergent, E., Baumgartner, R., and Bordet, F. <i>Bull. et mem. Soc. med. d. hop. de Paris</i> 50: 20, 1926	3	Spontaneous pneumothorax and mediastinal emphysema, on table of anesthesia, hemorrhage, 24 hours	1 day
Zodek	5	Pneumonia or spread of tuberculosis	?
Herben, G. L. <i>Personal communication to the author</i>	2	Mediastinal hemorrhage	?
Miller, J. A. <i>Personal communication to the author</i>	1	Pneumonia	Several weeks
Thomopoulos, A. <i>Paris</i> , 1925	1	Hemorrhage from pericardio-phrenic artery	?
Berry	1	Pneumonia and edema	24 hours
Total	26		

examination three days later revealed the heart pulled even more to the right than formerly and the trachea markedly deviated to that side. The diaphragm could not be seen, because a dense shadow obscured the diaphragm and lung on the right, except for the cavity in the upper lobe, which now appeared more sharply defined than previously.

On physical examination, there was marked dullness over the right side of the chest, but the breath sounds were clearly heard. X-ray films merely confirmed the fluoroscopic observations. Symptomatically, the patient was perfectly comfortable. She did not do well, however, and in August, 1929, had a profuse hemoptysis, after which the signs of a large antrum in the lower lobe of the right lung appeared. In December, 1929, roentgenograms still showed a massive atelectasis on the right and now some fresh infiltration in the left upper lobe. Bronchoscopic examination showed a marked angulation of the right main bronchus, and the mucosa of the bronchus of the middle lobe was swollen and

bled easily. This obscured the picture, but it was thought that there was in addition a definite obstruction in the bronchus of the lower lobe. At present the patient is at home and gradually going downhill.

It would appear that phrenicectomy in this case, for some unexplained reason, caused a massive atelectasis of the homolateral lung which was accompanied by almost no symptoms, but which, nevertheless, has resulted in a steady progression of the disease. It was advocated here as a test operation before and as an aid to thoracoplasty, but the outcome was poor.



Fig 1 (case 1)—*A*, before phrenicectomy *B*, after phrenicectomy. Massive atelectasis is present.

CASE 2—M I, a woman, aged 30, had a history of "bronchitis" for several years with two hemoptyses, one in 1922 and the second in 1928. She had taken rest treatment intermittently, and for nine months previous to her admission to the Fifth Avenue Hospital, in January, 1929, had noticed some pain in the lumbar region. Roentgenograms of the lungs and back revealed an extensive fibrocaceous tuberculosis of the right lung with cavities in the upper lobe and considerable fibrosis in the lower lobe. On the left side there was early infiltration in the upper lobe and some thickening about the hilus. Also, there was partial destruction of the third and fourth lumbar vertebrae and the intervertebral disk. At that time the patient was raising about 120 cc of sputum a day. She was in bed on a Bradford frame from Jan 17 to June 5, 1929. From May 24 to June 5, she had daily hemoptyses varying in amount from 50 to 500 cc, and on June 1, was given a transfusion of 300 cc of blood. Right phrenicectomy was performed on June 5.

with the hope that the bleeding might be arrested. At that time the temperature averaged from 99 to 100 F, the pulse rate was from 90 to 120, and respiration, 26. Immediately following operation there was dyspnea with a pulse of from 120 to 140 and a respiratory rate of 32 and later 40. There was a rise in temperature to 101 F, and twenty-four hours later a drop to 97 F. Cough and sputum diminished markedly at once. Her physical signs, however, were those of steadily increasing moisture throughout both lungs, and medium and coarse râles could be heard everywhere. The dyspnea and râles increased, she became cyanotic, and finally died forty-five hours after operation.

In this instance phrenicectomy was advised almost as a last measure. The disease had already lighted up and was progressing rapidly with daily large hemoptyses. It was hoped that phrenicectomy might control these. Instead, her already delicate cardiorespiratory balance was upset and her ability to cough hindered, with resultant prompt bronchiogenic spread and death.

CASE 3—C. B., a man, aged 35, had had tuberculosis for five years. The lesion was extremely fibroid and was confined entirely to the right lung, chiefly the upper lobe. There were two small cavities at the apex and tremendous fibrosis with marked retraction of the heart to the right, pulling up of the right side of the diaphragm and pronounced displacement and angulation of the trachea. In fact, the pull on the trachea was so marked that the patient became dyspneic on relatively slight exertion. In addition, exercise produced occasional small hemoptyses. The temperature varied between 98 and 99 F, the pulse rate was 90, and the respiratory rate, 18. Phrenicectomy was performed on March 6, 1930. The dyspnea increased immediately, and the hemoptyses continued. The temperature rose to 101 F for forty-eight hours, the pulse rate was 100 and the respiratory rate from 26 to 30 for five days. Roentgenograms showed diffuse shadows all over the right pulmonic field, the trachea even more deviated to the right than formerly and the heart entirely within the right side of the chest. The symptoms gradually cleared up, so that there was eventually less dyspnea than before operation, and x-ray films showed a disappearance of the atelectasis with a return of the heart and mediastinum to their former positions. Nine weeks after operation, the patient's condition was about the same as before the phrenicectomy.

In this case phrenicectomy was performed to lessen the dyspnea and hemoptysis. A temporary atelectasis appeared on the operated side without untoward results. So far, however, there has been no benefit.

CASE 4—M. K., a girl, aged 19, had had fibroid phthisis of the lower lobe of the left lung for two and a half years. In November, 1929, an acute lesion developed in the upper lobe of the right lung. This gradually responded to absolute rest but late in February, 1930, a cavity appeared in the old process in the left lower lobe. She was in excellent condition, with a temperature of only 99 or 100 F. It was felt that a phrenicectomy was indicated and would be most beneficial. This was done on March 14. That evening she was somewhat dyspneic and her temperature was 102 F. The following morning her temperature was 105 F, the pulse rate, 150, and respiration, 30. Over the left lower lobe there were marked dulness and complete absence of breath sounds and râles. A diagnosis of massive atelectasis of the left lower lobe was made, and confirmed later by a roentgenogram.



Fig 2 (case 4) —Before phrenicectomy There is a healing lesion on the right with fibrosis, and a cavity in the left lower lobe

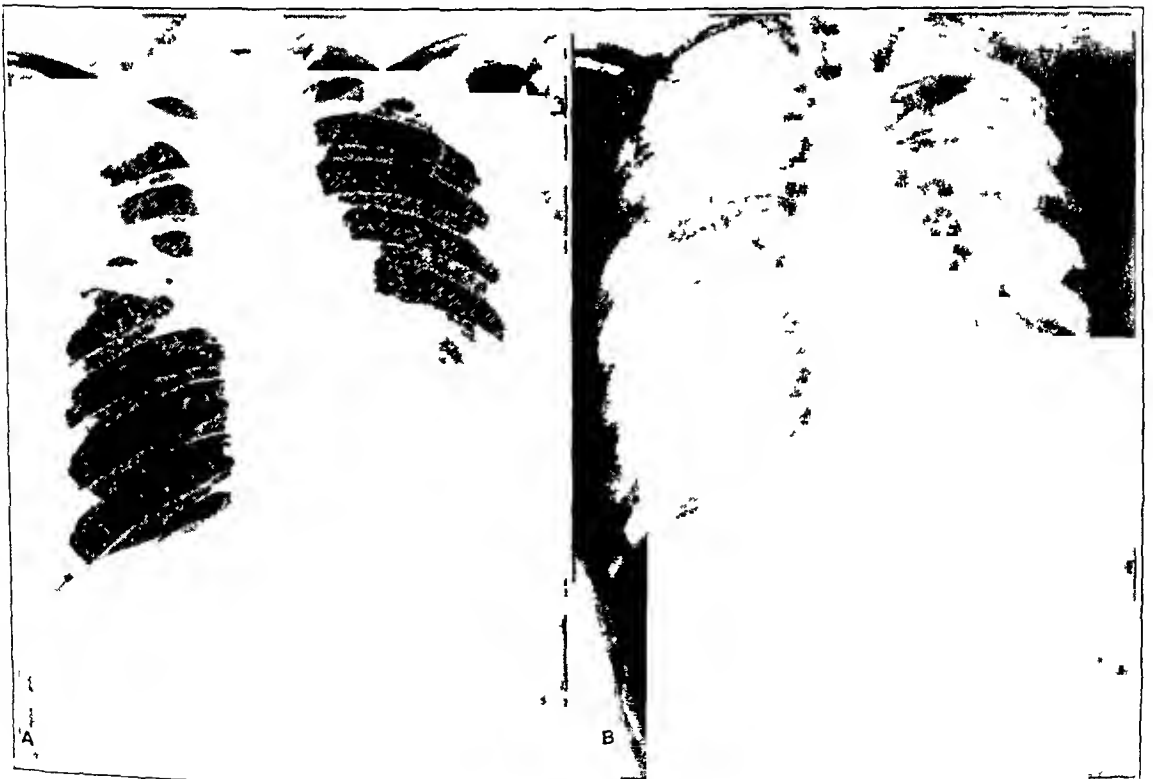


Fig 3 (case 4) —*A*, twenty-four hours after operation There is massive atelectasis of the left lower lobe *B*, forty-eight hours later The atelectasis has cleared up, with a return of the mediastinal structures to their normal positions  
Bronchopneumonia

The next day dulness was less and breath sounds and râles could be heard over the affected lobe, twenty-four hours later a second x-ray film showed an apparent bronchopneumonia of this portion of the lung. The heart had returned to its normal position, and the lung appeared well aerated. After about a week her temperature, pulse and respiratory rates came down, and she improved steadily. Bronchoscopy was not performed, because she never looked as ill as her pulse and temperature seemed to indicate, and she was always able to cooperate well and to cough freely.

In this case I felt that the collapse of the lower lobe immediately following phrenicectomy was so great, owing to the high rise of the diaphragm, that there was temporary interference with the drainage of the cavity and a resulting plugging of the bronchus of the lower lobe with thick secretions. Atelectasis developed, with a sharp general reaction. This soon cleared, however, but was followed by a mild bronchopneumonia, fortunately with rapid improvement.

#### SUMMARY

I have endeavored to point out that there is a definite risk associated with crushing, resection or avulsion of the phrenic nerve. Fifty-seven cases, four of which are my own, have been reviewed in which phrenicectomy was most detrimental, twenty-six of the patients died as a result of the operation. These poor results have all been subsequent to properly performed operations without technical error. In view of the fact that there is such widespread advocacy of phrenicectomy as a harmless procedure in cases of pulmonary tuberculosis, bronchiectasis and even abscess of the lungs, it would seem wise to sound a word of caution and to call attention to the risk involved, slight though it is.

#### CONCLUSIONS

How may these accidents be avoided? As to the selection of cases, Dumarest and Berard<sup>12</sup> have mentioned that there is less danger of mishap in cases that have become more or less stabilized. Patients in whom the disease is acute and progressive do not respond so well. Case 2, in which the patient died, is an example of this.

Another group of patients who may have trouble are those with large amounts of sputum, as in bronchiectasis, or an extensive fibrocaseous type of tuberculosis, in which it is essential for drainage that coughing be free and unobstructed. Phrenicectomy does not always facilitate cough and expectoration, occasionally, it works just the other way. This is well demonstrated by the case of bronchiectasis reported by Sergeant, Baumgartner and Boidet,<sup>6</sup> again by case 2, and more recently by a patient of Dr. James A. Miller<sup>13</sup> with bronchiectasis. Operation so

<sup>12</sup> Dumarest and Berard, L. *Rev de la tuberc* 9 161, 1928

<sup>13</sup> Miller, J. A. Personal communication to the author

hindered cough and drainage, with resultant decrease in sputum, that the secretions puddled in the lung, and an extensive fatal pneumonia developed. I therefore feel that phrenicectomy is a serious procedure in this type of case also and should not be undertaken without full realization of the possible consequences.

With the foregoing facts in mind, it may be possible to eliminate some of these unfortunate complications. It is not my wish to detract in any way from the value of phrenicectomy or the great benefits derived from it in all properly selected cases. I wish merely to place before the medical profession the fact that there is a certain risk (12 per cent) of poor results associated with it, and a mortality of about 0.5 per cent.

Finally, is it not possible that perhaps these figures do not represent all of the unfavorable results and fatalities that have followed phrenicectomy?

# MECHANICS OF COLLAPSE THERAPY AND ITS INDICATIONS

OBSERVATIONS IN SEVEN HUNDRED CASES

E J O'BRIEN, M D

DETROIT

Among thoracic surgeons and others interested in the treatment for pulmonary disease, there still seems to be a divergence of opinion as to the mechanics involved in collapse therapy. My only justification in presenting this paper, which dwells chiefly on the fundamental principles involved in these procedures, is to present my deductions on the subject, based on observations on 700 operative cases. I hope that it will bring out discussion that may lead to a better understanding.

While in a few patients with pulmonary tuberculosis the lesions heal by resolution, as do those in nontuberculous pneumonia, by far the greater number heal after the formation and contraction of newly formed fibrous, connective tissue has caused their encapsulation. Rest to the lung, by causing a slowing of the lymph flow and a retarded circulation, results in a lessened toxemia and an increased production of this fibrous tissue. By prohibiting this rest and unfavorably influencing the closure of cavities when they exist, the normal respiratory cycle retards rather than promotes healing of these lesions as becomes apparent when one reviews the physiology of respiration.

## MECHANISM

While the mechanism involved in the respiratory cycle is complicated, the underlying principles are simple. In the normal condition, except for enough fluid to moisten their surfaces the lungs completely fill the thoracic cage, and as a result the elastic tissue with which they are supplied must be stretched sufficiently to accomplish this. Because of this elastic tissue, the lungs are constantly tending to contract and collapse away from the thoracic wall, but there is an adhesive force between the parietal and visceral pleura which keeps these surfaces in contact.

The result of these two forces is a tension which is called negative pressure, less than atmospheric pressure. During inspiration, the thorax is enlarged and the tendency is to pull the thoracic wall away from the lung, which act, of course, must increase this intrapleural negative tension and stretch the elastic tissue of the lung still further as more air is sucked down the trachea to fill the air spaces. The diaphragm is the chief muscle that enlarges the thorax from above downward whereas

the enlargement in the transverse diameter is accomplished by the elevation of the ribs. The muscles chiefly involved in this are the external intercostals and the serratus posticus superior. Other accessory muscles are also used.

Expiration is mostly a passive phenomenon. When the inspiratory muscles cease to contract, the thorax sinks and is diminished in size. This allows the elastic tissue of the lung to contract and reduce its volume. This constant activity of respiratory movements greatly interferes with perfect rest for lesions in the lung. During rest in bed, the respiratory rate is reduced, and as there is no need for excessive inspiratory movements to enlarge the thorax, the resultant quiet breathing affords some rest and reduction of lung volume, which explains the efficacy of this form of treatment in pulmonary disease. Unfortunately, in a large number of patients with pulmonary tuberculosis the rest thus afforded is not sufficient to allow healing, and additional rest must be given. That collapse therapy is so rapidly coming into extensive use in the treatment for this disease is readily understood when one bears in mind that it is the only method of securing this added rest.

Artificial pneumothorax (by reducing intrapleural negative tension), operations on the phrenic nerve (by paralyzing the diaphragm) and thoracoplasty (by removing the rigid, bony support of the thoracic wall and impairing the functions of inspiratory muscles) diminish the size of the hemithorax or the space in which the lung moves, and allow still further relaxation of elastic tissue, reduction in lung volume and limited inspiratory excursion. Rest is measured in direct proportion to this limitation.

I believe that in most instances surgical procedures act in a passive way by relieving an active inspiratory menace and result merely in an exaggerated expiration. For this reason, I prefer to use the term collapse or relaxation therapy rather than compression therapy in relation to these measures. That they do act in this manner is clear because they do nothing to the lung itself but merely overcome the untoward effects of the respiratory cycle and of the structures surrounding the lung which are preventing it from contracting of its own accord.

With pneumothorax, one can cause almost complete collapse of the lung and this is done under negative tension in most instances. Here it is obvious that there could be no compression.

During thoracoplastic operations, the lung can be seen to contract and collapse as soon as the rigid, bony wall which has been preventing it from doing so is removed. The amount of collapse allowed by this procedure is usually in direct proportion to the amount of ribs removed. That this is true is borne out by the fact that the Brauer operation in which large lengths of rib are removed causes more reduction in lung volume than does the Sauerbruch operation in which only small seg-



ments are removed, and also by the fact that with anteiolateral thoracoplasties, in which the remaining portions of ribs are removed, still greater reduction in volume is accomplished. That actual pressure is not exerted on the lung in these patients has been proved by the readings of intrapleural pressures following thoracoplasty. These readings were found to be negative. This, then, is also relaxation.

Operations on the phrenic nerve accomplish a similar result. The diaphragm is paralyzed, loses its muscle tone and ceases its movements. It becomes thin and fascia-like, which makes it more susceptible to intra-abdominal and intrapleural pressures. This results in its being sucked up higher into the thorax by the negative tension existing there, causing reduction in the size of the hemithorax from above downward, which releases the elastic tension in the lung in direct proportion to its elevation.

I believe that actual compression is exerted only when pneumothorax is carried on to a positive pressure or when direct pressure is made over a cavity wall by using muscle or some foreign substance as a packing as is done in apicolysis and other forms of extrapleural pneumolysis. That the weight of the soft tissues overlying the lung after thoracoplasty and the intra-abdominal pressure following phrenicectomy cause some pressure is probable, but as the lung, because of its elastic tissue, recoils and contracts away from these forces, there can be no pressure unless it occurs after the lung has been fully contracted. This condition, however, rarely exists.

If a cavity exists in pulmonary tissue, there is no natural tendency for it to close, as the act of inspiration, by enlarging the thorax and stretching the elastic tissue surrounding the cavity tends to enlarge it, and these procedures which release elastic tension and allow the lung to contract assist in the cavity's closure. In principle, this closure of cavities in the lung by surgical procedures is analogous to the simple experiment of making a hole in a piece of rubber tissue. If the rubber is stretched, the hole becomes larger, if it is relaxed, the hole becomes smaller.

Whether or not cavities within the substance of the lung and surrounded by alveolar and elastic tissue will close on release of elastic tension following surgical measures, depends on several factors: first, the size of the cavity and the amount of reduction obtained in the size of the hemithorax and the volume of the lung, and second, the thickness of the cavity wall, those with thick walls being much harder to close than those with soft walls. We surgeons have seen thick-walled cavities displaced but unchanged in size even with marked contraction of the lung around them. Sometimes even actual compression fails to close them.

Cavities situated at the periphery of the lung and in which the cavity wall is in direct contact with the parietal pleura are also hard to close, as there is no elastic tissue surrounding them which can contract and help in their closure when the tension is released. These may be closed by a complete collapse of the lung by pneumothorax, which may have to be carried on to a positive pressure, or, if they are situated at the apex of the lung as is usually the case, they may be closed when phrenic operations have caused a reduction in the size of the hemithorax, and the contracted lung, in adjusting itself to the reduced space, migrates upward away from the ascending diaphragm in the line of least resistance. If these cavities are situated at the base of the lung, with the wall resting on the diaphragm, direct relaxation of their wall with possible obliteration may take place when this muscle is paralyzed.

When the cavity wall is adherent to the thoracic wall, it may be necessary to perform thoracoplasty which will remove the rigid, bony framework that tends to keep the cavities open and allow a relaxation of the cavity wall to occur. All pulmonary cavities, wherever situated, are, of course, favorably influenced by this procedure, because it causes marked diminution in the size of the hemithorax and the volume of the lung. Thick-walled cavities at the periphery of the lung are almost as difficult to close as are those situated within the substance of the lung, as their walls do not collapse readily.

#### INDICATIONS

Which of the many surgical procedures is to be used in any given case is often difficult to determine. In the *Journal of the American Medical Association* of Feb 9, 1929, and in the November issue of the same year of the *American Review of Tuberculosis*,<sup>1</sup> I published papers in which I discussed fully the indications for each procedure from the anatomicopathologic characteristics of the lesion, and these articles may be referred to for my views on these points. After carefully analyzing my experiences and results in the large number of patients referred to in the title of this paper, I have changed my views only in extending my indications and am now employing these procedures in a wider range of patients, more especially in those with bilateral tuberculosis.

It is no longer necessary to defend these procedures, but the extent to which they should be used is still a question of debate, many physiotherapists still being conservative about them and others wishing to employ them in almost every suitable case. There can be only two reasons for not immediately instituting some form of surgical collapse for

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<sup>1</sup> O'Brien, E. J. Surgery of Phrenic Nerve and Intrapleural Pneumolysis, *J. A. M. A.* **92** 463 (Feb 9) 1929, *Am. Rev. Tuberc.* **20** 787, 1929.

unilateral lesions, one being that the lesion is so small that one is optimistic enough to believe it will get well on rest in bed alone, the other, that such a measure could not help. In my opinion, the latter reason would apply only to patients with a pneumonic or consolidated lung or with other complications that would make collapse of the lung seem useless.

One has so often seen rapid increase in small lesions which one hoped could be healed by ordinary rest in bed that this type of lesion is now looked on with more suspicion. It is a benign lesion indeed in the treatment of which I do not feel that at least a crushing of the phrenic nerve should be resorted to in order to give the patient the benefit of the additional rest afforded while the diaphragm is paralyzed. In my experience, even in this group of patients, the time allowed before the diaphragm resumed its function was not sufficient to cause complete healing, and the nerve usually had to be removed later.

There can be no question but that collapse therapy in some form should be used when ordinary rest in bed and other accepted methods of treatment have been tried and the lesion is not healing. As there should no longer be a question of the merit of these procedures, if they are not to be used more extensively, it must be on the ground that they are too great a risk to the patient or too great a burden on the contralateral lung.

The mortality from phrenic operations is, of course, negligible. In my experience, the mortality from thoracoplasty is about 6 per cent. In my opinion, this mortality rate in the class of patients in which these measures are indicated, argues for, rather than against, a more extensive use of collapse therapy.

A large percentage of my patients have had bilateral lesions, and my observations have been that, in a good percentage of these, the disease in the contralateral lung has healed along with that in the side on which operation was performed, showing that no so-called "added burden" had been placed on it. I have not been convinced that any of these measures have been the direct cause of spread or activation of disease in the other lung. These constantly occur in patients under routine treatment by rest in bed, and I have seen patients in whom the lesion spread to the good lung between the time it had been decided to operate and the time the operation was to have been performed. If these patients had been operated on, the operative procedure would have been blamed. I have seen lesions or so-called "spreads" occurring after operation that have cleared up promptly in spite of the surgical procedure on the opposite side that was supposed to have been their cause.

There is, as a rule, a greater tendency to contraction in the diseased area than in normal lung tissue, and I often obtain a selective collapse without much loss of alveolar function. While the normal person has a much larger amount of alveolar space than is necessary to carry on life, there is in most cases a compensatory hypertrophy of the other lung following collapse therapy. This does not mean that an added burden is thrown on the disease in that lung, but rather that more air cells are being used than previously.

In the attempt to understand more clearly just what does take place following collapse therapy, I studied a series of patients on whom phrenicectomy had been performed. Dr. Weiner presented a paper at the National Tuberculosis Society at Memphis this year in which complete observations, taken at regular intervals until the vital capacity returned to normal, were recorded. It was found that following phrenicectomy there was an immediate decrease of about 32 per cent in the vital capacity in all patients. In all but one patient, the tidal air decreased. The consumption of oxygen, however, remained practically unchanged. This, of course, necessitated some compensatory mechanism. The compensation was found to take place in three different ways with practically an equal number of patients in each group. In group I, the compensation was achieved by an increase in the respiratory labor only. In group II, the compensation was achieved by a better utilization of the inspired air, with no change in the respiratory labor, and in group III, it was accomplished only by a more efficient utilization of oxygen, with a decrease in the respiratory labor. There was no evident correlation between the extent and the pathologico-anatomic type of the lesion and the mechanism of compensation following the operation. The fact, therefore, that following phrenicectomy over two thirds of the patients achieved compensation for this reduction in vital capacity without increased respiratory rate means that an added burden is not thrown on the lesion in the other lung, but that probably an increased circulation in the contralateral lung accounts for both the better utilization of oxygen and the improvement usually seen in lesions existing in this lung. It may be significant to note that in about 70 per cent of my operative cases the lesions in the contralateral lung improved. This percentage is practically that of the two groups in which better utilization of oxygen was achieved without increased respiratory labor.

That there is a compensatory hypertrophy of the contralateral lung following collapse therapy, however, is shown by Sieper,<sup>2</sup> in an article

<sup>2</sup> Sieper, H. Die Vitalkapazität bei der Lungenphthise besonders bei der Lungencollapstherapie, Beitr. z. Klin. d. Tuberk. 65 725, 1927.

published in 1927 in the *Beitrage zur Klinik der Tuberculose und spezifischen Tuberkulose-Forschung*. The author had a pneumothorax of the right side performed on himself. He found that the drop in vital capacity after each inflation of air was equal to the volume of air introduced into the pleural cavity, as long as the intrathoracic pressure was kept within moderate limits. After the initial drop, the vital capacity increased during collapse. The increase was definitely faster than the resorption of intrapleural air, and it reached the original level before the pneumothorax was completely resorbed. After the resorption of the pneumothorax, the vital capacity was greater than before the treatment. Sieper attributed the increase in vital capacity to the depression of the diaphragm and increase in the circumference of the thorax or, in other words, to hypertrophy. In patients with pulmonary tuberculosis, the vital capacity following the inflation of air is greater than the difference between the original vital capacity minus the inflated air. This fact is explained as follows. The pulmonary tissue surrounding tuberculous foci frequently does not participate in the aeration process. The vital capacity of such a patient is, therefore, smaller than could be expected from the size of his foci. The collapse of such areas does not decrease the vital capacity of the patient. It follows that the vital capacity after the induction of pneumothorax will be higher the more damaged tissue is collapsed in proportion to normal tissue.

It is apparent, therefore, that while under collapse therapy the diseased area does not require the utilization of compensatory mechanism, but that under any form of collapse therapy some normal lung tissue is usually collapsed which necessitates such compensation. This compensation therefore takes place, as has been explained, but it does so without throwing an added burden on the lesions existing in the contralateral lung.

As no procedure or treatment will cause all lesions to heal, these lesions sometimes continue to increase on the collapsed side, it is not surprising, therefore, that lesions in the opposite lung also become worse. However, this does not warrant the assumption that collapse therapy has had a deleterious effect on them.

It must be understood that collapse therapy in any form is not curative but merely puts the patient in the most favorable condition for healing. The use of this procedure on patients who are obviously not doing well and the following immediate improvement prove only that this therapy has a distinct value in the arrest of the disease, such results do not justify a belief that collapse therapy should be used only in this group of patients.

As inherited resistance to this disease plays an important part in the success of any treatment, the employment of surgical procedures is not as effectual in the Mexican, the Indian and the Negro as in other races, and it is more often in this type of patient that so-called "spreads" are found

Obviously, collapse of the lung should not be instituted if the fields of both lungs are so involved with disease and the vital capacity is so low that the patient's respiratory ability might be endangered. However, even if there is considerable disease, with cavitation, in the contralateral lung, collapse therapy may be begun on the other side if it seems advisable. This is possible because of nature's generosity in providing a superabundance of alveolar space and because of the passive action of these procedures. Partial bilateral collapse may also be instituted without endangering the patient, if carried on carefully. The performance of phrenicectomy on one side and pneumothorax on the other is not an uncommon procedure. Bilateral pneumothorax is coming into general use and even bilateral phrenicectomy has been performed on a considerable number of patients without deleterious effects. I think it is advisable in bilateral tuberculosis, however, to begin collapse therapy on the side most affected, as this alone is often sufficient to cause healing of lesions in both lungs.

I believe that when collapse therapy is employed in bilateral tuberculosis, the healing of lesions and the closure of cavities in the contralateral lung are due partly to an increased blood supply to this lung, partly to the lessened toxemia and general improvement of the patient when the side most affected is under treatment, and partly to the stoppage of drainage from the cavities. Shifting of the mediastinal structures to this side with the resulting release in tension is also a factor.

It is surprising that it has taken so long to realize what an integral part of the treatment for pulmonary tuberculosis surgical procedures should be. We have all seen many patients in whom nature has attempted to accomplish the same result by shelving the ribs and narrowing the rib spaces, elevating the diaphragm, pulling over the mediastinal structures, etc., in an effort to reduce the volume of the hemithorax by contraction of the fibrous tissue which had been formed in the attempt at healing. To assist this attempt is, in our minds, the sole purpose of surgical procedures.

When a patient with pulmonary tuberculosis is presented for treatment, the first question should be whether or not some surgical procedure might be of benefit. Of course, many patients will be found in whom such measures will not be indicated. If the patients have early minimal lesions which are improving, it may be decided to give rest in

bed a short trial, or if the disease is far advanced in both lung fields or many complications exist, surgical intervention may seem useless. However regardless of the result obtained in individual cases, I feel that the mechanics involved clearly indicate that the reasons for employing these measures are fundamentally sound and that until some future scientist discovers a specific cure, the treatment for pulmonary tuberculosis must be surgical, in conjunction with rest in bed and routine methods.

### ABSTRACT OF DISCUSSION

ON PAPERS BY DRS HEDBLOM, BERRY AND O'BRIEN

DR HOWARD LILIENTHAL, New York, Dr Hedblom made a convincing point in showing what can be done after the failure of the ordinary posterior thoracoplasty. I heartily approve of this method. I believe that the general method was initiated by Dr Welles, and I have used it with modification.

Dr Berry's paper was scholarly and extraordinarily interesting. I had the impression that unfavorable results following the operations for blocking of the phrenic nerve were uncommon. It is most important to bear the possibilities in mind. I certainly shall never again tell a patient that operation on the phrenic nerve can do no harm.

There is another point. In the sequence of operations, I think that it is improper to cause blocking of the phrenic nerve before the establishment of pneumothorax, especially in suppurative disease. In tuberculosis, perhaps, exceptions may be possible, because I have seen the following thing happen. A patient with a bronchiectatic suppuration in the lower lobe had refused to have a lobectomy performed, although she had had the disease a long time, and lobectomy was clearly the best choice. I said, "Let's take out your phrenic nerve."

She said, "Go to it, that's nothing."

I did. I obtained a good elevation of the diaphragm, and the condition of the patient was improved. I said, "Now we will put in some air and get more compression." I neglected to bear in mind the fact that blocking of the phrenic nerve is followed by paralysis and flaccidity of the diaphragm. When Dr Wessler introduced pneumothorax, he pushed the diaphragm down lower than it was before the operation. I enjoyed Dr O'Brien's paper, and I am going to read every word of it. He has emphasized an important fact, and that is that there is not an operation for tuberculosis, but that there is a surgical treatment for tuberculosis. The medical profession should be informed on this subject, for nearly every physician thinks only of one operation—thoracoplasty. Concerning the motion of the lungs of which Dr O'Brien spoke, please bear in mind that the motion of the lungs that one sees when the ribs have been cut is a paradoxical motion. When the patient exhales, his lung expands, and when he inhales, the lung tends to collapse. The picture that was taken on the way to the operating room was undoubtedly taken during full inspiration and thus opened the abscess cavity so that it showed very well in the picture. On the way from the operating room the picture was also taken in full inspiration, but the cavity was then closed because the paradoxical motion of the diaphragm and the sucking up of the diaphragm into the chest produced its obliteration temporarily. The abscess cavity was not really and permanently closed.

DR E. ARCHIBALD, Montreal, Canada. I should like to say a few words concerning Dr Hedblom's paper. It is timely, I think, that Dr Hedblom should bring

forward the advantages of the second operation, or perhaps, in Dr Hedblom's graded plan, the sixth or seventh operation, of anterolateral costectomy.

I failed to gather, however, from his paper that he had made any real distinction between the early and the late operation. He included some cases of pyopneumothorax in which the removal of the ribs anterolaterally would be considered as part of the whole procedure and would therefore be done early, because one cannot close large tuberculous empyema cavities without taking off practically all the ribs from front to back and top to bottom. That has been done for a good many years. He included others, however, in which anterolateral thoracoplasty was performed months or more after the primary posterior thoracoplasty. The distinction is important. The chief indication I believe for anterolateral costectomy lies in the group in which there are cavities remaining unclosed by the usual posterior operation. This point was made by Dr Welles, of Saranac Lake, two or three years ago, in an article in the *American Review of Tuberculosis*. One should be able to judge such cases from the start and say to the patient, "You will not get your cavities closed by the ordinary posterior thoracoplasty. You will need a further stage of the anterolateral type."

I think that is what we should aim at—the conception of an early anterolateral costectomy for patients in whom the cavity is not closed by the posterior operation. I could not gather whether or not Dr Hedblom intended to make this point in his paper. I have carried it out in a few instances lately. I have performed late secondary operations for years, on the whole without much benefit. Too much fibrosis and reformed bone prevent further collapse, but from this earlier anterolateral costectomy I am getting encouraging results.

DR L. T. LEWALD, New York. There is a complication that I have seen in a case referred to me by the New York Health Department, in which an operation on the phrenic nerve had been performed the year previously for a tuberculous lesion in the left lung (fig A). Excessive elevation of the diaphragm followed the phrenicectomy. The patient complained of the same symptoms that I have seen in eventration of the diaphragm which has not resulted from paralysis of the diaphragm in the sense that it is postoperative, but a spontaneous eventration due in some cases to congenital absence of the musculature of the diaphragm so that the diaphragm being more or less immobile, causes the trapping of gas in the cardiac end of the stomach and the lower end of the esophagus is below the level of the gas and consequently the patient cannot eruct the gas.

This patient now complains bitterly of the gastric distress so that I feel that occasionally it would be unwise to bring about a paralysis of the diaphragm on the left side.

The slide shows the stomach filled with gas and opaque material, and in the lateral view, the diaphragm can be seen elevated to an enormous height and the stomach below it unable to expel the gas through the esophageal orifice. On the right side one would not have to consider this complication. I do not know whether this condition has been observed before and whether it is really of sufficient importance to make it unwise to operate unless the condition of the lung is sufficient to warrant the danger of this unpleasant after-result.

DR CARL A. HEDBLOM, Chicago. Dr Berry's paper is certainly a most important contribution to the subject of phrenicectomy. The operation is generally characterized as simple and harmless, with the interence that it may be performed by operators with meager experience and for slight indications. Dr Berry's series of cases is large enough to show conclusively that serious complications may result. I have had two patients in whom Horner's syndrome developed. I



am of the opinion that if the nerve cannot be definitely identified without undue effort, it is better to abandon the attempt than to do harm

The roentgenogram made after the use of iodized oil is an indispensable guide for the prognosis following phrenicectomy. Bilateral involvement seems to me, generally speaking, a contraindication. Cylindrical bronchiectasis, especially of the distal bronchi, in my experience, offers the best prognosis.

The distinction between the terms collapse and compression seems to me of no great importance. In many cases following extensive thoracoplasty there is a decided shifting of the heart toward the opposite side, which would seem to me to indicate that the lung is compressed. We have had cases in which the shifting of the mediastinum has been complicated by pleural effusion. In such cases the manometer has shown positive pressure after thoracoplasty, causing dyspnea and necessitating the withdrawal of fluid.



Eventration of the diaphragm following phrenicectomy

DR FRANK B. BERRY, New York City. We agree with Dr. Lilienthal as to the advisability of pneumothorax preceding a phrenicectomy in bronchiectasis, as we feel that a great deal of information can be gained and that accidents can perhaps be avoided.

DR E. J. O'BRIEN, Detroit. It seems to me that we are laying too much stress on the dangers of phrenicectomy without bearing in mind just why we are doing it. I do not think that any person would have a phrenic nerve removed instead of going to an afternoon tea. It is removed because the patient has pulmonary tuberculosis or an equally serious disease.

If one accepts the statistics of Naveau, Barnes and others who show that a tuberculous patient with cavity and positive sputum has only a 5 per cent chance of living longer than five years, an occasional accident during the performance of the operation might be excused. I think that we lose sight of the results of the procedure in talking so much about the ill effects.

Readings of intra-abdominal pressure are not as negative as those of intra-thoracic pressure, and one notes intra-abdominal pressure from the viscera in the prone position

Regarding Dr Hedblom's observations about the shifting of the mediastinal structures, I have seen that happen time and again under negative pressure during pneumothorax treatment when there could not possibly be compression. When pneumothorax is being administered and the pressure is negative, the mediastinum often shifts. I do not think, therefore, that the shifting of mediastinal structures which occasionally follows thoracoplasty indicates that compression is made by this procedure.

# AMEBIC HEPATIC, SUBPHRENIC AND PULMONARY ABSCESES \*

STUART W HARRINGTON, M D

ROCHESTER, MINN

The occurrence of amebic dysentery in the temperate zones is rare when compared with its occurrence in the tropical zone. It has been only in recent years that the disease has been recognized with any frequency in patients who have not been in the tropics. Amebic abscess is one of the most common complications of amebic dysentery. Rogers<sup>1</sup> stated that acute amebic dysentery usually presents scattered lesions in the bowel and multiple abscesses in the liver. In chronic cases, the lesions are less extensive and may involve only a small part of the bowel. In these cases the abscesses in the liver are usually large and single and the intestinal disorder is often latent, with no clinical manifestations. It is generally accepted that the amebas pass from the ulcerated areas of the bowel, through the portal vein to the liver. In acute cases, amebas in great numbers, often associated with pyogenic bacteria, reach the liver. Inflammation of the vascular walls, clotting and multiple hepatic abscesses result. The occurrence of a large solitary abscess usually is found in cases of slight or latent amebic colitis. Solitary abscesses may be sterile, and their formation differs from the multiple abscess type in that comparatively few amebas reach the liver. When a sufficient number of amebas has reached the liver to cause clotting in some of the small vessels so that the blood supply is interfered with, sufficient necrosis is produced to permit escape of the amebas through the vascular walls, into the necrotic hepatic tissue, and a solitary abscess is produced. This abscess develops in a concentric manner, and if the patient survives long enough, a fibrous capsule develops around it. It is in the wall of the abscess that the amebas are found. *Endamoeba histolytica* is usually obtained from scrapings from the walls of the cavity, not from the thick pus from the abscess cavity. Rogers found the ameba in the pus in four of eighteen surgical cases in which he conducted the examinations and in the scrapings of the wall of the cavity in seventeen of the cases.

My experience in the treatment of amebic abscess is limited to five cases in which I have operated in the last five years. My purpose in reporting these cases is to show that although the occurrence of amebic

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From the Division of Surgery, the Mayo Clinic

1 Rogers, L. Amoebic Liver Abscess. Its Pathology, Prevention and Cure. *Lancet* 1 463, 569, 677 (March 11, 18, 25) 1922, *Brit M J* 1 224, 264, 345 (Feb 11, 18) 1922

abscess in the temperate zones is uncommon as compared with that in the tropical zone, it is not rare, and also to point out the frequency with which the symptoms in this group of cases of amebic hepatic abscess were thought to be due to primary pulmonary or pleural disease. In the five cases here reported, an initial diagnosis of a pulmonary lesion was made in four. In the fifth case, a definite diagnosis of amebic dysentery was not established until five months after the onset of the disease. An abscess of the liver developed even though the patient was given extensive treatment with emetine.

The usual symptoms in cases of amebic abscess are diarrhea, fever, chills or sweats, occurring some time in the course of the disease. Pain in the right hypochondrium is usually present. Preceding diarrhea is often the only symptom that is significant of the probable etiology. Ludlow<sup>2</sup> stated that it is present in nine of ten cases, although it may have occurred years before the abscess appears. He also wrote, "many of the patients presented a septic condition so often observed in cases of chronic empyema," and he called attention to the special diagnostic sign of deep-seated pain in the region of the abscess, elicited by a sudden thrust with the end of the finger.

In the five cases here reported, four patients gave histories of diarrhea, but in only one case was it a prominent factor in the complaint. In three cases, it was difficult to elicit any history of diarrhea, for the patient had not attached any significance to it and had not mentioned it in stating the history of his complaint at the time of examination. In the remaining case, a history of diarrhea was not obtained.

In one case, the patient contracted amebic dysentery in the tropics. In the remaining four cases, a history could not be obtained of the patients having been out of the north temperate zone. In two cases there was a history of alcoholism.

The importance of early diagnosis cannot be overestimated, for the prognosis is good if treatment is instituted early, before the additional complication of rupture through the liver and diaphragm into the lung has occurred. In these five cases, the abscess was confined to the liver in two cases, and in both it was a large solitary abscess. In two cases, the abscess had ruptured through the liver into the subphrenic space. In the remaining case, an abscess presented in the upper lobe of the right lung, which was undoubtedly secondary to an abscess of the liver. It was impossible to determine definitely whether this abscess was the result of direct extension from the hepatic abscess by rupture through the diaphragm into the lung or whether the amebic infection was transmitted to the lung through the blood stream, the invading organisms having passed from the hepatic abscess into the inferior vena cava.

<sup>2</sup> Ludlow. A. I. Amebic Liver Abscess. *China M. J.* 40: 1165 (Dec.) 1926.

to the right side of the heart, and through the pulmonary arteries to the lung. Brown<sup>3</sup> reported a similar case in which he thought that the pulmonary abscess resulted from deposition of amebas by the blood stream, metastatic from the abscess of the liver. This view, he felt, was substantiated at necropsy, because an opening through the diaphragm connecting the liver with the pulmonary abscess was not demonstrable. MacNeal and Klemperer<sup>4</sup> reported a case of amebic abscess which was complicated by multiple small abscesses in both lungs, and from the microscopic examination of the tissue removed at necropsy they concluded that the amebas had a tendency to penetrate the blood vessels and were disseminated by way of the blood stream from the liver, thence to the right side of the heart and pulmonary arteries to the lung. In the case of extension to the lung, which I am reporting, there was response to treatment, and there was no definite way of determining the method of transmission of the amebas to the lung. Nevertheless, the clinical history indicated that extension to the lung was probably brought about by direct transmission through a rupture of the diaphragm.

The surgical treatment should be as conservative as possible and should be combined with adequate administration of emetine. Rogers advocated repeated aspiration and injection of solutions of quinine into the abscess cavity, but omitted the injections of quinine after the introduction of treatment by emetine. He stated that amebic or tropical abscess of the liver is usually an easily preventable disease, and that the occurrence of amebic suppuration in the liver should cause serious consideration by the physician in whose hands it had been allowed to develop.

Ludlow stated that each case of hepatic abscess must be treated according to the condition found, that no hard and fast rule can be made for every case, but that in practically all cases some form of surgical treatment is required besides medical treatment. He also stated that repeated aspirations and subcutaneous injections of emetine is the method of choice, but that in many cases open operation and drainage are required.

The usual procedure is as follows. A preliminary course of emetine (0.06 Gm.) is given by daily subcutaneous injections for from two to four days before operation if the patient's condition will permit delay of surgical intervention. The abscess is then aspirated, the site of aspiration depending on the most likely situation of the abscess, as determined by general examination. The most usual site is the ninth

3 Brown, R. Amoebic Abscess of Liver with Pulmonary Sequelae, California State J. Med. **19** 282 (July) 1921.

4 MacNeal, W. J., and Klemperer, P. Amebic Abscess of the Liver, Am. J. Trop. Med. **5** 339 (Sept.) 1925.

interspace in the anterior axillary line. If the location of the abscess is not definitely determined by examination, this site is usually selected for aspiration. The aspirating needle should not be inserted for a depth of more than from 5 to 7 cm. If pus is obtained, a small trocar and cannula is inserted into the abscess, under local anesthesia. A small puncture of the skin with a knife often facilitates the introduction of the trocar and cannula. As much of the pus as possible is removed at the first aspiration. If the pus is thick, a catheter may be inserted through the cannula and the cavity irrigated with a surgical solution of chlorinated soda (Dakin's solution), or it may be necessary to resort to open operation. The aspirations are repeated when the patient shows signs of reaccumulation of pus in the cavity. This depends, to some extent, on the size of the abscess. In large abscesses, there is often rapid reaccumulation of bloody serum after removal of the pus. If the patient does not respond to treatment by emetine, and if the clinical data indicate the presence of an abscess of the liver which cannot be located with the aspirating needle without danger of injury to the lung and pleura, or to the abdominal viscera, it is best to perform exploration of the abdomen. If an abscess is found at exploration, it can be treated either by an open operation or by closing the abdomen without drainage and performing a secondary window operation over the cavity of the abscess for subsequent drainage by aspiration. Subcutaneous injections of 0.05 Gm of emetine are continued until the patient receives from six to ten doses. This is usually sufficient, but if symptoms recur, a second course of treatment by emetine should be given.

#### REPORT OF CASES

CASE 1—A man, aged 23, a resident of Indiana, consulted the clinic on June 2, 1928, because of pain in the right lower part of the thorax, of twelve weeks' duration. He stated that his illness began following unusual exposure to cold weather, when pain developed in the right lower portion of the thorax. On the following day, he noticed slight fever but continued to work. There was no cough or hemoptysis, but there was loss of appetite and weight. His condition was thought to be due to tuberculosis, and he was sent to Texas. A roentgenogram of the thorax did not show evidence of tuberculosis, and his condition was then thought to be due to gastric ulcer. He returned home to Indiana and for the three weeks previous to his coming to the clinic had been confined to bed, with severe pain in the upper right portion of the abdomen, lower part of the thorax and right lumbar region. The temperature rose as high as 102 F in the afternoon but usually did not go above 100 F. He also had occasional night sweats which were severe. He had lost from 20 to 30 pounds (9 to 13.6 Kg) in weight in the twelve weeks previous to his visit to the clinic. The pain in the right lower part of the thorax had been severe enough for codeine to be required for from two to three weeks prior to examination. He had vomited three or four times and complained of considerable nausea after eating. He was constipated. He had never had diarrhea at any time, and during his illness, had required a daily enema. He was admitted to the hospital as an emergency case.

General examination revealed evidence of marked emaciation. The cheeks were flushed. The margin of the liver was not palpable, there was a slight tenderness in the right upper part of the abdomen and the right lumbar region. Examination of the thorax gave essentially negative information. The systolic blood pressure was 104 and the diastolic, 70 mm of mercury. The pulse rate was 120 each minute. The temperature was 99.6 F at 2 p. m. The urine contained a few granular casts and a few pus cells, but was otherwise negative to examination. The concentration of hemoglobin was 64 per cent, erythrocytes numbered 4,010,000, and leukocytes 30,500 in each cubic millimeter of blood. The differential leukocyte count was as follows: lymphocytes, 16 per cent, large mononuclears, 7.5 per cent, transitionals, 2.5 per cent and neutrophils, 74 per cent. The Wassermann reaction of the blood was negative. Repeated examinations of stool before operation did not disclose amebas, ova, pus or blood. A roentgenogram of the thorax gave evidence of marked elevation of the right side of the diaphragm. A diagnosis of right subphrenic abscess was made, and exploration was advised.

On June 6, 1928, the right, subphrenic space was found to be negative to several aspirations made through the tenth and eleventh interspaces. Because of the patient's progressive symptoms it was thought best to perform abdominal exploration, and a large, solitary abscess of the liver was found, involving about a third of the right lobe. The hepatic abscess was aspirated, and about 5 cc of thick, bloody, greenish puslike material was removed. This was immediately taken to the laboratory, and *Endamoeba histolytica* was found to be present. A section of the ninth rib and cartilage were removed, in the anterior axillary line, immediately over the abscess cavity, and a stab wound was made through the posterior periosteum. A strip of gauze was placed in the stab wound and down to the lateral surface of the liver in the abscess cavity. The abdominal wound was closed without drainage. The patient was given treatment by emetine hydrochloride, and on the following day the gauze was removed and the cavity was aspirated through the stab wound in the thoracic wall. About 150 cc of amebic material from the liver was removed. This was done on three occasions at intervals of three and four days (fig 1).

There was moderate shock immediately following the abdominal operation. The temperature and pulse were normal on the fifth day, and from that time on convalescence was uneventful. Examination of the stool four days after the operation revealed cysts of *Endamoeba histolytica*. The patient was dismissed from observation one month after operation, at which time he had gained about 20 pounds (9 Kg), and his condition was good. He had had no fever from the fifth day after operation, and his wounds were entirely healed.

*Comment*—The onset, in this case, followed considerable exposure, and suggested pulmonary disease, which was thought probably to be tuberculosis. Tuberculosis was soon ruled out, and the later symptoms were characteristic of subphrenic or hepatic abscess. The patient had not lived outside of the north temperate zone and he had never had any attacks of diarrhea. Although amebic hepatic abscess was suspected clinically, the examinations of stool before operation proved negative for *Endamoeba histolytica*. The preliminary aspiration was performed with the hope of establishing a definite diagnosis without more radical surgical intervention. Aspiration in the right subphrenic and hepatic spaces gave negative results because the abscess was deep

lying, and more anterior than posterior. When exploration of the abdomen was carried out and the diagnosis was established it was thought best to treat by repeated aspiration rather than by open drainage, because of the danger of secondary infection which takes place under conditions of open drainage and also because the patient had never received treatment by emetine. It was thought that he would respond more satisfactorily to repeated aspiration than to emetine and this was substantiated by his rapid response to treatment and his complete recovery.

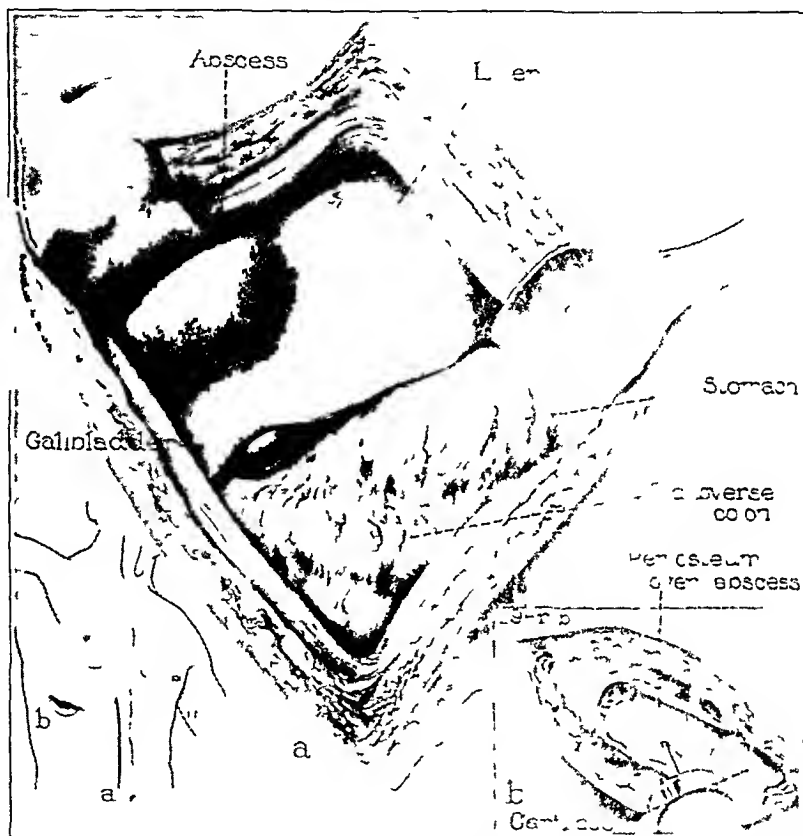


Fig 1 (case 1) —*a*, large amebic abscess of the right lobe of the liver. *a'*, site of incision, *b*, resection of the anterior segment of the ninth rib for subsequent aspirations, *b'*, site of incision.

CASE 2—A man, aged 37, a resident of Michigan consulted the clinic on Feb 20, 1929, because of pain in the upper right part of the abdomen which was referred to the upper portion of the thorax and because of loss of weight and strength of three months duration. Four years prior to his admission while he was in Florida, diarrhea had developed and he had passed from three to four stools a day. This continued for about four months when the diarrhea became so severe associated with blood in the stool that it was necessary for him to go to a hospital. He had daily rise in temperature, he had lost from 20 to 30 pounds in weight and had lost strength. Numerous tests had been made but nothing definite had been found and his condition was thought to be due to a lesion of the hepatic flexure. One month later a diagnosis of amebic dysentery was made.



and emetine was administered with immediate response and apparent recovery. Six months later he had recurrence of diarrhea, associated with bearing-down pain in the rectum, weakness and loss of weight. Emetine was again administered with less rapid response. He then continued to have recurrence of symptoms every four or five months. Emetine was given with each attack, but each time the treatment seemed less effective in relieving symptoms. About one year previous to admission, while in Brazil, he had a recurrence of former symptoms, with a temperature of from 100 to 102 F. He was given emetine and chiniofon, N N R and five injections of neoarsphenamine. During this illness, pain developed in the right lower part of the thorax and upper right part of the abdomen. At first the pain was dull. After two weeks, the pain disappeared and the temperature gradually returned to normal. For one month following this, he gained in weight and strength, and after two months he returned to work. Almost immediately after he returned to work he began to have fever daily, it gradually increased in severity until it reached 104 F in the afternoon. He was given a course of acetarsone and emetine, with gradual improvement of symptoms, until he felt quite well after a period of three weeks. Four months before he came to the clinic, he suddenly lost appetite, fever again developed, with pain in the right lower part of the thorax and abdomen, moderate diarrhea and gradual loss of weight and strength. This condition had become progressively worse until the time of his admission to the clinic. He had lost 35 pounds (15.9 Kg) in weight during the four months before his admission.

General examination revealed marked loss of weight. The systolic blood pressure was 94 and the diastolic, 64. The pulse rate was 105 and the temperature was 101 F. Examination of the right side of the thorax disclosed dullness to percussion, anteriorly to the fourth interspace, and posteriorly to the sixth thoracic vertebra. The margin of the liver could be felt from four to five fingerbreadths below the right costal margin, with marked bulging of the lower right portion of the wall of the thorax. Urinalysis gave negative results. The concentration of hemoglobin was found to be 45 per cent, erythrocytes numbered 3,340,000 and leukocytes, 10,600 in each cubic millimeter of blood. The differential leukocyte count was as follows: lymphocytes, 21 per cent, large mononuclears, 1 per cent, neutrophils, 77 per cent, eosinophils, 1 per cent. There was marked anisocytosis and poikilocytosis. Repeated examinations of stool were negative for *Endamoeba histolytica*. Roentgenograms of the thorax gave evidence of marked elevation of the right side of the diaphragm, with some thickening of the pleura (fig 2A). A diagnosis of amebic abscess of the liver was made, and operation was advised.

On February 26, the right subdiaphragmatic space was aspirated through the tenth interspace in the posterior axillary line, and about 2,200 cc of typical amebic pus was removed from the liver. The fluid was light chocolate-colored, and was streaked with thick puslike material and particles of hepatic tissue. This fluid was sent for examination and was found to be negative on culture. Amebas were not found. Following operation, emetine hydrochloride was given. The abscess cavity was again aspirated, March 4, at which time 800 cc of the same type of material was removed. The patient did not receive much relief from pain from the second aspiration, and it became progressively more severe. On March 7, a third aspiration was performed with a needle of large caliber, and only a small amount of thick, degenerated material was removed. Because of the patient's poor general condition and the inability to obtain pus by aspiration, it was thought best to resort to open operation. A small portion of the eleventh rib was removed with the idea of draining the subphrenic space. After a segment of the rib had been removed, it was found that the right pleural phrenic space was not oblit-

erated, and that there was a small amount of fluid in the pleural cavity probably resulting from previous aspirations. It was thought best not to attempt to drain the abscess through the pleural space, and the wound was closed. Abdominal exploration was then performed, and a huge, solitary, amebic abscess was found involving two thirds of the right lobe of the liver. The abscess cavity contained about 500 cc of thick, bloody, degenerating hepatic tissue. Examination of the scrapings from the wall of the cavity showed *Endamoeba histolytica* to be present. The necrotic material was removed, and the large cavity in the liver was packed with gauze.

There was considerable shock following the operation, after which the patient was given emetine hydrochloride subcutaneously. The gauze was completely removed by the tenth day, after which a tube was inserted and the cavity was irrigated throughout his convalescence with saline and surgical solution of chlorinated soda (Dakin's solution). The patient was dismissed from the hospital on the twentieth day, and from observation about two months after the operation.

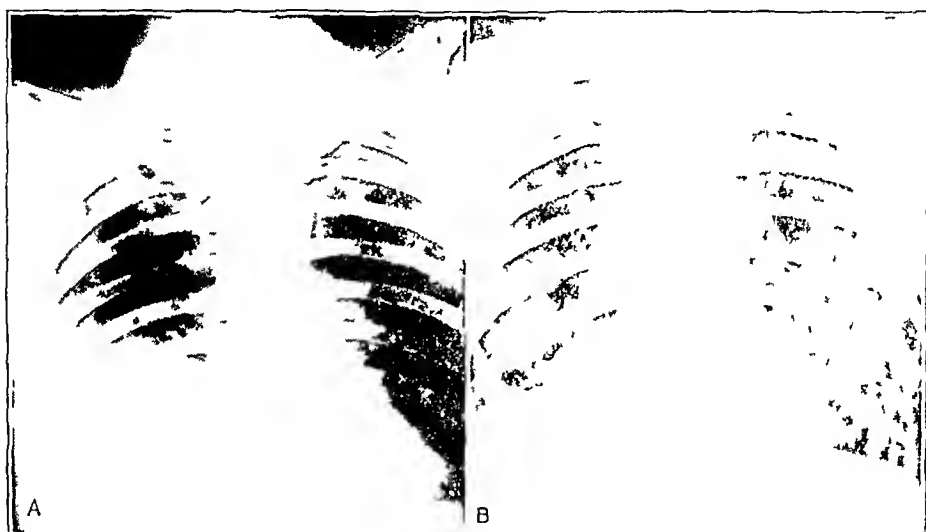


Fig 2 (case 2) —A, roentgenogram on admission showing marked elevation of the right side of the diaphragm with some thickening of the pleura. B roentgenogram on dismissal showing pleuritic adhesions at the right costophrenic angle, and slight elevation of the right side of the diaphragm, the lungs were normal.

At the time of his dismissal, the cavity in the liver had become practically obliterated. There remained a small sinus in the abdominal wall. The patient had gained 25 pounds (11.3 Kg) in weight and his general condition was good (fig 2B).

*Comment*—The amebic abscess in this case developed in the liver while the patient was under intensive treatment with emetine and *Endamoeba histolytica* was absent in repeated examinations of stool. It will be recalled that lack of response of the patient to conservative treatment by aspiration and inability to continue it because of the thick necrotic material in the abscess cavity necessitated the institution of open surgical drainage. However the costophrenic angle of the pleura was not walled off because the abscess was confined to the liver and

had not ruptured into the subphrenic space. Consequently, abdominal drainage was carried out. From the symptoms, it is evident that the patient had been suffering from abscess of the liver for a year before he came to the clinic. I think it advisable to institute early drainage of the abscess in cases of this type, when the condition does not respond to the more conservative types of treatment.

CAs. 3—A youth, aged 17, a resident of Michigan, consulted the clinic on July 7, 1925, because of pain in the right lower part of the thorax, of three months' duration. He stated that he had been well until about one year before admission when he began to feel tired and to lack ambition. In the last year he had had more or less chronic cough. He had had one severe spell about one year before he came to the clinic. The onset of his present complaint, three months prior to admission, was characterized by cough, fever and a general feeling of malaise. The condition had been diagnosed as influenza, and he had recovered in about a week and had returned to work. He soon had a relapse, with chill, high fever and pain in the right lower part of the thorax. From that time, until he came to the clinic, he had had a constant afternoon rise in temperature, ranging between 102 and 103 F. For ten days prior to admission, he had had nausea, with some vomiting, and the pain had extended into the right flank and right upper quadrant of the abdomen. Pain had been severe at times. He had had considerable urinary frequency, particularly at night, for three to four months previous to his visit. He had always been constipated. On further questioning, after a diagnosis had been established, he stated that he had had one short spell of diarrhea two months previous to admission, with from three to four stools a day over a period of four or five days. He had lost 12 pounds (5.4 Kg.) in weight in the three months before admission.

General examination gave evidence of loss of weight and pallor of skin indicating a rather marked degree of anemia. The breath sounds over the right base were impaired, there was bulging of the interspaces and marked tenderness of the right lower part of the thorax. Urinalysis gave essentially negative results. The concentration of hemoglobin was 35 per cent, erythrocytes numbered 2,380,000 and leukocytes 12,400 in each cubic millimeter of blood. The color index was 0.5. The differential leukocyte count was as follows: lymphocytes, 27 per cent, large mononuclears, 35 per cent, transitionals, 15 per cent, and neutrophils 68.0 per cent. The Wassermann reaction of the blood was negative. Repeated examinations of stool were negative for amebas. Roentgenograms of the thorax gave evidence of elevation of the right side of the diaphragm to the level of the fourth rib anteriorly. Roentgenograms of the colon were negative. A diagnosis was made of subdiaphragmatic abscess of uncertain origin, and operation was advised.

On July 23, the right subphrenic space was first aspirated, and encysted thick, bloody, greenish material was obtained and was sent for examination and culture, with negative results. Incision was made through the intercostal space and about 1,500 cc of thick, bloody, puslike material, with very pungent odor which seems characteristic of amebic pus, was drained from the large abscess cavity. The ameba was found in material scraped from the wall of the abscess cavity. The cavity was packed with a strip of iodoform gauze, and treatment with emetine and acetarsone was instituted.

Immediate convalescence was stormy for the first two weeks, after which the patient's condition began to show some improvement. This, however, was of short duration, and after one week he again began to have an elevated temperature.

with some diarrhea *Endamoeba histolytica* was found in the stool and a second course of treatment by emetine was instituted. His general condition again improved moderately, but there was continued loss of appetite and progressive loss of strength. The diarrhea did not respond to administration of emetine or to other treatment. His condition became gradually worse until his death on the forty-fourth day. The cavity of the subphrenic abscess became progressively smaller from the time treatment was begun until his death at which time it had a capacity of less than 30 cc. At necropsy it was found that the subphrenic abscess had practically healed. There was marked ulceration of the colon and terminal bronchopneumonia.

*Comment*—The course of this patient's illness was insidious and probably extended over several months before the definite event which simulated influenza, occurred three months before his admission. The periodic attacks of cough with pain in the right side of the thorax suggested a primary thoracic lesion and the recurrence of the attacks suggested a complicating abscess. It was difficult to establish a definite diagnosis because of the absence of any definite history of diarrhea, and because of the absence of *Endamoeba histolytica* in the stool. The lack of response to treatment was undoubtedly due to the extremely bad condition at the time treatment was instituted. The patient's death was due to inanition as result of colitis.

CASE 4—A man, aged 38, a resident of Iowa, consulted the clinic on Aug. 5, 1929, because of morning cough and a draining sinus in the right side of the thorax. Except for chronic morning cough in 1927 he had been well previous to September, 1928, at which time he became ill and his condition was diagnosed as pneumonia involving the right lung complicated by jaundice and pleural effusion. Clear, pleural fluid was aspirated many times in the first three weeks of his illness. At the end of the third week the fluid became purulent and a rib was resected in October, 1928. He had had a draining sinus in the right lower part of the thoracic wall since that time. On second questioning a more detailed history of his complaint was obtained. He then stated that for three years prior to his admission to the clinic, he had had a cough with a moderate amount of sputum usually only in the morning. One and a half years prior to admission he started having spells of weakness which necessitated his stopping work for a day or two at a time. There was gradual loss in weight and strength and progressive morning cough for a period of three months when he first noted pain in the upper right quadrant of the abdomen. He became jaundiced and this was accompanied by diarrhea and passage of green watery stools. For the first two days he had from ten to twenty stools a day. The stools then became normal and very light and putty-like in color. The condition remained about the same for from six to seven days when he had sudden pain in the right side of the thorax, severe chills with fever, and marked perspiration which lasted until morphine was given. He was sent to the hospital and a diagnosis of pneumonia of the right lung was made. The jaundice cleared up in about two weeks and the stools became colored after about three days. One week after the admission of the patient to the hospital the right side of the thorax was aspirated and about 2 liters of clear fluid was removed. The aspirations were repeated every two to three days for the next three weeks when the fluid became purulent and one rib was resected for drainage. The patient did fairly well until about one year prior to admission when he

again began to have fever with slight chills. This subsided with increased drainage from the sinus in the right lower portion of the thorax. He had had repeated similar attacks in the year prior to his visit to the clinic, which would disable him for from a few days to a week at a time. The bowels were normal, and he had no cough or expectoration in the year previous to his admission. He had lost 60 pounds (27.2 Kg) in weight during the year.

Results of general examination were essentially negative, except that it disclosed marked loss of weight and abnormalities in the right side of the thorax. The urine was normal. The concentration of hemoglobin was 35 per cent, erythrocytes numbered 3,800,000 and leukocytes 7,400 in each cubic millimeter of blood. The color index was 0.6. The Wassermann reaction of the blood was negative. Examination of the pus discharged from the sinus of the right side of the thorax did not disclose sulphur bodies or actinomycosis. Roentgenograms of the thorax revealed evidence of elevation of the diaphragm on the right side with a fluid level beneath, suggesting an old subphrenic abscess. Operation was advised.

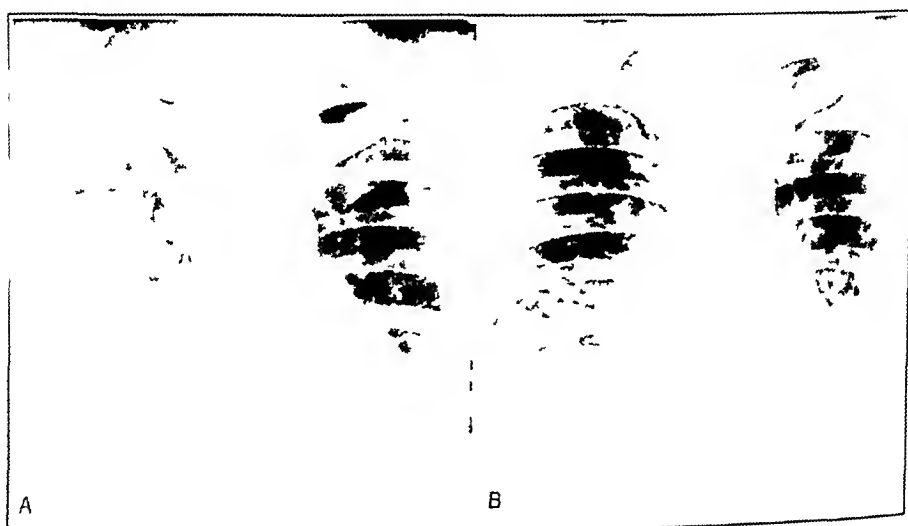


Fig 3 (case 4) — *A* roentgenogram on admission showing fluid at the base of the right lung apparently below the diaphragm, the fluid level at the tenth rib, posteriorly, partial collapse of the lower right lobe and enlargement of the heart graded 1. *B*, roentgenogram on dismissal showing moderate elevation of the right side of the diaphragm and slight interlobar pleurisy, the lungs were normal.

However, the patient refused to be operated on and went home. He returned to the clinic on December 30, as his condition had been getting progressively worse since his previous visit (fig 3*A*). He had been unable to do any work in the interval.

On Jan 4, 1930, a tube was inserted into the draining sinus in the right lower part of the thorax, and about 700 cc of reddish-brown, thick, purulent material with fetid odor, was removed. This was found to contain *Endamoeba histolytica*. Drainage of the subphrenic abscess was established in one stage by resection of 7.5 cm of the tenth and eleventh ribs in the posterior scapular line. The cavity held about 900 cc of this same reddish-brown, purulent material. On exploration of the cavity, it was found that the sinus tract, which led to the right lower lateral thoracic wall was very tortuous and opened into the extreme anterior angle of the subphrenic abscess, at which point it had penetrated the diaphragm.

Convalescence was uneventful. The temperature dropped to normal on the fourth day. The patient was dismissed from the hospital on the fourteenth day, at which time the wound was in excellent condition, and there was a large residual cavity which was filling in rapidly. The patient was dismissed from observation six weeks after the operation, at which time the cavity was almost completely obliterated, and his general condition was excellent. He was given two courses of emetine during convalescence and had gained 15 pounds (6.8 Kg) in weight, with marked increase in strength. He returned for observation three months after operation, at which time his general condition was very good. The concentration of hemoglobin was 60 per cent, and he had gained 40 pounds (18.1 Kg) in weight. The operative wound and the old sinus in the anterior thoracic wall had

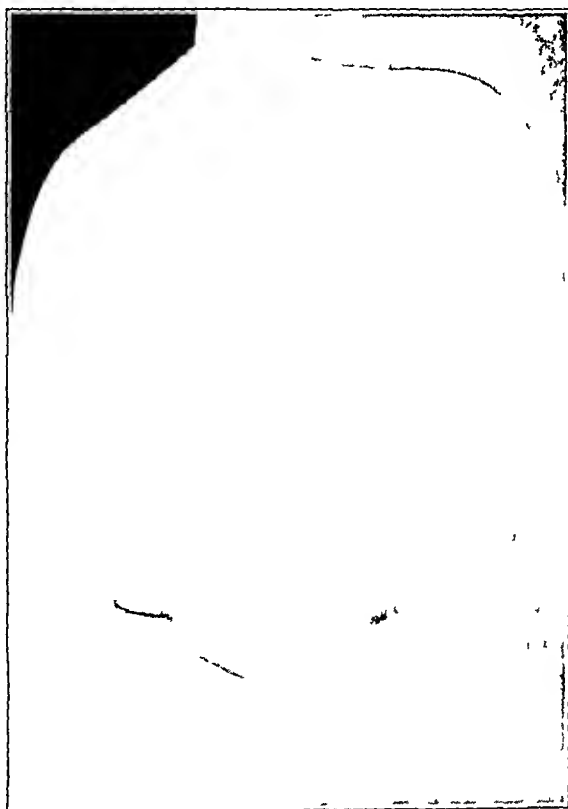


Fig 4 (case 4) —Old sinus in the right side of the thoracic wall, and recent operative wound entirely healed on patient's dismissal, condition excellent, gain of 40 pounds in weight

entirely healed. The roentgenogram of the thorax gave evidence of elevation of the right side of the diaphragm to the fourth rib and did not reveal abnormality in the lungs (figs 3B and 4)

*Comment* —This patient stated that he had always lived in a temperate zone and had never been south of Iowa. He had been troubled more or less with diarrhea since he was a small child and therefore attached no significance to the more recent attacks of diarrhea. The severity of his illness, simulating pneumonia is rather unusual. Probably the original condition was abscess of the liver which had

ruptured into the subphrenic space, at that time causing the marked prostration. The progressive dyspnea probably resulted from a complicating pleural effusion due to the subphrenic abscess. The first aspirations undoubtedly drained this secondary clear pleural effusion. The later aspirations probably penetrated the diaphragm. Then, as resection was of the ninth rib in the midaxillary line, and as the diaphragm was markedly elevated the subphrenic space was entered instead of the pleural cavity, and thus the extreme anterior portion of the abscess cavity was drained. Open surgical drainage was necessary because of the secondary infection of the amebic abscess and because of the patient's extreme illness.

CASE 5—A man, aged 25, a resident of Indiana, consulted the clinic on Dec 6, 1928, because of loss of weight and hemoptysis of five weeks' duration. About three months prior to admission, he noticed pain in the right posterior portion of the thorax with afternoon fever, loss of appetite, general weakness and loss of weight. A week or so later he first noticed a nonproductive cough. About two months before he came to the clinic, after he went to bed, he coughed up some blood. He consulted a physician, and a diagnosis of fluid in the right side of the thorax was made. Diagnostic aspiration was done, at which time a small amount of bloody, purulent material was obtained. A few days later, resection of a rib, with drainage of the right pleural cavity was done. There was some improvement in his condition, but the cough continued, became progressively worse, and was accompanied by considerable bloody expectoration. There was little drainage from the thoracotomy wound, which had practically closed. Because of his cough, bloody expectoration and loss of weight, a malignant condition of the lung was thought to be present.

At the time of admission to the clinic, the patient was weak and emaciated, and was sent immediately to the hospital. He stated that previous to the onset of pulmonary symptoms, he had had loose, watery stools, probably three or four times a day. He did not think much about this. There was no pus or blood in the stools. While in the hospital, six weeks before he came to the clinic, his condition had become worse and had remained so for four weeks while he was there. On dismissal, two weeks before he was seen at the clinic, his condition was improved, but his symptoms recurred on admission to the hospital after he had come to the clinic.

General examination revealed marked emaciation, with loss of about 35 pounds (15.9 Kg) in weight. The systolic blood pressure was 120, and the diastolic 80. The pulse rate was 150, and the temperature at 4 p. m. was 101 F. Examination revealed dulness, with decreased breath sounds and decreased fremitus over the entire right side of the thorax, posteriorly. There was a healed scar in the right side of the thorax, posteriorly. Urinalysis gave essentially negative results, except that it revealed a few pus cells. The concentration of hemoglobin was estimated at 45 per cent, erythrocytes numbered 3,310,000 and the leukocytes from 14,800 to 28,100 in each cubic millimeter of blood. Examination of the sputum for bacilli of tuberculosis, spirilla and fusiform bacilli gave negative results. The stool contained *Endamoeba histolytica*. Roentgenograms of the thorax revealed evidence of a thickened pleura at the right base, with a fluid level at the fourth rib (fig 5A). A diagnosis was made of amebic abscess of the lung, secondary to a ruptured abscess of the liver, and operation was advised.

On December 8 the right thoracic cavity was aspirated, and a small amount of thick, bloody, greenish pus was removed. This was found to contain *Endamoeba histolytica*. The stool obtained on the same day contained *Endamoeba histolytica*. Two courses of emetine and a product similar to acetarsone were given. The patient's condition immediately began to improve. He continued to have considerable cough and expectoration and roentgenograms of the thorax disclosed a shadow in the region of the right lower lobe, posteriorly. It was thought that this was either a walled-off pocket in the pleura or an abscess of the lung, and operation was advised. On December 15, posterior thoracotomy was performed, and a small pleural pocket containing about 30 cc of thick, purulent material was found, into which opened several bronchial fistulas, with a large necrotic mass in the right middle lobe of the lung. A portion of this necrotic pulmonary tissue was removed for better drainage and the cavity was packed with iodoform gauze. The necrotic material removed from the wall of the abscess in the lung contained amebas. Two subsequent courses of the aforementioned drugs were given.



Fig 5 (case 5) —A, roentgenogram on admission showing increased density over the entire lower right portion of the thorax, elevation of the diaphragm (?), fluid (?) B, roentgenogram one month after drainage of an amebic abscess in the lower portion of the right lung, dense infiltration of the base, and elevation of the right side of the diaphragm

The patient's condition continued to improve satisfactorily. He was dismissed from observation on the forty-eighth day after operation, at which time his general condition was satisfactory. He had gained 26 pounds (11.8 Kg) in weight and there was marked improvement in strength. The thoracotomy wound had practically healed. A roentgenogram of the thorax disclosed dense infiltration at the right base and elevation of the right side of the diaphragm (fig 5B).

*Comment*—This case was diagnosed successively, as primary intrathoracic disease empyema and a malignant condition of the lung. The attack of diarrhea at the time of the patient's admission to the clinic suggested the possibility of an amebic abscess of the liver which had ruptured through the diaphragm. It is unusual to find amebas in the pus which is removed from the thoracic cavity.



## ABSTRACT OF DISCUSSION

DR L T LEWALD, New York I should like to show several slides illustrating the difference between a subphrenic lesion and a pleural lesion

In the case (for a report and illustration of the case see *Subphrenic Abscess and Its Differential Diagnosis Roentgenologically Considered*, ARCH SURG 10 544 [Jan] 1925) illustrated in this slide I had previously examined the patient on account of a subacute abdominal condition on the right side, which may have been due to appendicitis About a month later, I saw this large fluid level lesion with some irregularity just above it My diagnosis was subphrenic abscess associated with slight pleuritic involvement, simply adjacent irritation through the diaphragm without any actual collection of fluid in the pleural cavity I had great difficulty in maintaining this diagnosis Two internists insisted that the fluid was in the pleural cavity Two surgeons also said the fluid was in the pleural cavity However, one surgeon agreed with me that it was a subphrenic abscess, which proved to be the case

I was particularly convinced by the lateral thoracic view, with a complete curve of the diaphragm, that the fluid was below the diaphragm I think that makes the differential diagnosis with absolute certainty The dome of the diaphragm is perfectly depicted following this line all the way back, and above that the slight pleural exudate on the diaphragmatic surface of the pleura

At the first operation, the surgeon who was not convinced that it was a subphrenic abscess did an open operation above the diaphragm and then inserted a probe with the idea that it would lead into the abscess cavity It did not, but went into the pleural cavity However, it did no harm, as the pleura was already infected Then at a subsequent operation an incision was made downward through the diaphragm, and the abscess was drained

Drainage was then instituted, and the patient made an excellent recovery I took a roentgenogram of him several months afterward, and the diaphragm remained slightly elevated, but the pleural lesion had entirely cleared up

I insist that direct lateral exposure is necessary in making a differential diagnosis in a case of this sort If oblique projection is used, the signs are difficult to interpret Oblique projection is useful at times and supplemental, but to see the dome of the diaphragm it is necessary to make a direct lateral exposure

# THE TREATMENT FOR PENETRATING WOUNDS OF THE PLEURAL CAVITY

DUFF S ALLEN, M D

ST LOUIS

The treatment for wounds that penetrate the pleura is diametrically opposed in many respects to the treatment for wounds that penetrate the peritoneal cavity. The treatment for wounds that penetrate the abdominal cavity usually is radically operative, for those wounds which penetrate the thoracic cavity, the conservative nonoperative treatment is often the best. The presence of blood within the abdominal cavity is of little moment. It may be left undisturbed. Blood left within the pleural cavity may lead to extensive empyema and death.

The surgical principles that govern the treatment for wounds of the peritoneal cavity cannot be applied to the treatment for wounds of the pleural cavity. This distinction is important. It saves life. If the surgeon performs an exploratory thoracotomy on the same premises that he does an exploratory laparotomy, for example, for a penetrating gunshot wound, many patients whose chests are explored will die who otherwise would not have died.

The explanations for this are based on five facts. 1. There are differences between the organs contained within the pleural, and those within the abdominal, cavity. 2. The pressures within the pleural cavity are maintained at a more negative level than are the pressures within the abdominal cavity. The natural tendency of the pleural cavity is toward the formation of cavities, the natural tendency of the abdominal cavity is toward their obliteration. 3. The pleural cavity seems to react to the presence of contaminated blood in a manner different from that of the peritoneal cavity. 4. It is impossible to bring the pleural cavities and the organs that they contain to a complete or even an effectual rest. 5. The blood pressure within the pulmonary circulation is only one-sixth the pressure within the systemic circulation. Bleeding is more easily controlled when it occurs from the pulmonary system than when it occurs within the abdominal cavity.

The recent World War afforded an unusual opportunity for the study of penetrating wounds of the chest. For the first time the modern surgeon, equipped with his present knowledge, could observe and treat such wounds in wholesale lots. Large defects in the chest wall were often seen as the result of shrapnel and pieces of high explosive.

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\*From the Department of Surgery, Washington University School of Medicine.

shells Of course, there were numerous bullet wounds of the chest that produced injuries similar to those met with in civil, or perhaps uncivil, life today

In the beginning of the war, wounds of the chest that did not produce immediate death were not considered unusually serious This idea was the result of previous experiences with wounds observed in civil life It was soon found, however, that the wounds resulting from shrapnel and high explosive shells were different from the wounds seen in civil practice

Bradford,<sup>1</sup> one and a half years after the beginning of the war, reported a series of about 500 cases of gunshot wounds observed in a base hospital The patients were first seen by him from two days to one or two weeks after injury Such cases, he found, were not attended by a high mortality He noted that 25 per cent of all cases of hemothorax following penetrating gunshot wounds showed infection He advocated aspiration of the hemothorax and simultaneous replacement of the volume withdrawn by oxygen The present report shows the beneficial effect of removal of the hemothorax, but the method of removal differs slightly from that used by Bradford He found only 1 case in which there was a fatal secondary hemorrhage in 500 cases of gunshot wounds<sup>2</sup>

Duval<sup>3</sup> collected from the literature a total of 3,453 cases, reported by 37 authors These wounds of the chest and lung were sustained in the war The mortality was found to be 20 per cent He found that hemorrhage and asphyxia due to large defects in the wall of the chest were the principal causes of early death

Certain definite procedures of treatment were evolved, both in the Allied Armies and in the Armies of the Entente Duval and his co-workers established elaborate surgical procedures for the treatment of extensive wounds of the chest This was essential to the treatment for war wounds In these cases the defect in the chest wall is often large and the wound in the lung is extensive These conditions seldom obtain in wounds of the chest acquired in civil life

Duval noted that simple bullet wounds were either immediately fatal or relatively benign It is important to recognize this in civil practice Experience leads one to believe that it is seldom necessary to operate on the ordinary gunshot and stab wounds of the pleural cavity

It is not my primary purpose in this paper to discuss the treatment for war wounds of the pleural cavity The foregoing comment was

1 Bradford, John Rose Gunshot Wounds of the Chest, *Lancet* **1** 227 1916

2 Bradford J R *Brit J Surg* **3** 247, 1915

3 Duval, Pierre *Les plaies de guerre du poumon*, Paris Masson & Cie

made for the purpose of contrasting such treatment with that necessary in the usual penetrating gunshot and stab wound met with in civil life. Admirable descriptions of the proper treatment for war wounds of the chest have been published by Lihenthal,<sup>4</sup> Duval,<sup>5</sup> Rudolf, Gask and Wilkinson,<sup>6</sup> and Roberts and Craig.<sup>7</sup>

Among the many other excellent articles dealing with the proper treatment for war wounds those of Lockwood,<sup>8</sup> Dobson,<sup>9</sup> Morelli,<sup>10</sup> Hutchinson<sup>11</sup> and Tuffier<sup>12</sup> summarize the treatments for the various types of injuries.

#### PRESIDENTIAL SERIES

This is a report of the study of 162 cases of gunshot and stab wounds of the chest. These patients had entered the Barnes Hospital or the St. Louis City Hospital shortly after they had sustained their injuries. They were all seen within the first four hours after injury except for two patients who entered the Barnes Hospital twenty-four and thirty-two hours, respectively, after injury.

Following these penetrating wounds of the pleura death occurs as a result of the immediate effect of bleeding and also as a result of the later complications. Foremost among the later complications is empyema.

Several years ago during an investigation of the etiology of empyema, I had occasion to observe a number of gunshot and stab wounds of the pleural cavity. My experimental work indicated that the presence of contaminated blood within the pleural cavity is likely to lead to the formation of empyema. From this experimental work I acquired a great deal of respect and concern for contaminated hemothorax. In

4 Lihenthal, Howard. Thoracic Surgery. Philadelphia, W. B. Saunders Company, 1925, vol. 2, p. 518.

5 Rudolf, R. D. Later History of Cases of Gunshot Wounds of the Chest with Retained Missiles, *Lancet* 2 709, 1917.

6 Gask, G. E. and Wilkinson, K. D. Penetrating Gunshot Wounds of the Chest and Their Treatment, *Brit. M. J.* 2 781, 1917.

7 Roberts, J. E. H., and Craig, J. G. The Surgical Treatment of Severe War Wounds of the Chest, *Brit. M. J.* 2 576, 1917.

8 Lockwood, A. L. Early Operative Treatment in Chest Surgery. *War Med.* 2 6, 1917-1918.

9 Dobson, J. T. Some Features of Gunshot Wounds of the Chest. *Brit. M. J.* 1 661, 1918.

10 Morelli, Eugenia. Contributo alla cura dell'empyema, *Policlinico (sez. med.)* 25 153, 1917.

11 Hutchinson. A Study of 450 Cases of Wounds of the Chest, with Special Reference to a New Method of Treatment for Infected Haemothorax. *Canad. M. A. J.* 8 972, 1918.

12 Tuffier, T. The Secondary Surgical Treatment of Chest Wounds. *War Med.* 2 16, 1917-1918.

every gunshot or stab wound of the pleura that I observed there was opportunity for the formation of a contaminated hemothorax. My efforts were directed, therefore, toward the prevention and removal of the hemothorax.

The idea of removal of the hemothorax is not new. It is practiced generally. During the World War it was found that the mortality was reduced about 15 per cent by careful attention to aspiration of the blood. A curious fact is that the blood does not clot readily within the pleural cavity. I have been able to aspirate blood as long as nine weeks after a patient received a gunshot wound of the chest.

There is a more simple way of removing the blood from the pleural cavity than by aspiration. It consists of closing of the wound in the wall of the chest and having the patient lie with the closed hole down, in the most dependent portion of the chest. The hemothorax will gradually leak out.

The following case is an example.

#### REPORT OF A CASE

S. C., entered the hospital on Oct. 28, 1923, at 10:50 p. m., with a history of having been shot with a pistol one-half hour before. He was conscious, bleeding from the mouth and thirsty. He answered questions intelligently.

On examination, a small round wound was visible in the lower portion of the right axilla at the level of the sixth rib. There was a larger wound in the midsternal line at the level of the third rib through which air was being sucked with each respiration. There was no marked bleeding from either wound. (The patient was lying on his back.) The pulse rate was 120, respirations 24 and temperature 37.4 C (99.3 F).

Fluoroscopic examination of the chest showed the side to be clear. The cardiac outline was not markedly enlarged, the shape of the pericardium was that of a normal heart. The right side of the chest was opaque throughout. When the patient was turned on the left side he complained of shortness of breath and the heart shadow moved toward the left. Hemothorax (and pneumothorax) of the right side of the chest was evident.

The percussion note was resonant in the left side of the chest. The con sound did not indicate pneumothorax of the left pleural cavity. The right side of the chest disclosed distant breath sounds, with some impairment but no flatness.

Immediately on the patient's entrance to the hospital he was given hypodermoclysis of 1,000 cc of physiologic solution of sodium chloride. The sucking wound of the chest was closed. He was turned on his right side and kept with the bullet wound down. Morphine,  $\frac{1}{6}$  gram, was given, and the dose was repeated during the night.

At 2:30 a. m., on October 29, the patient was found to be bleeding profusely from the wound beneath the right axilla. A pressure bandage was applied (note by Dr. Deakin). At 3:30 a. m., he was still bleeding from the wound in the chest wall (Dr. Deakin). During the night the temperature rose to 103.6 F. At 8:00 a. m., examination showed the blood pressure to be 98 systolic and 40 diastolic, the temperature was 39.6 C (103.1 F) and the pulse rate 122. The rate of respiration was 40. The respirations remained stationary, the blood

pressure had fallen, and the pulse rate remained stationary. On the same day Dr. Singer saw the case and made the following note: "There is no evidence of hemothorax. Considerable interstitial emphysema throughout the right chest extending down to abdomen. Left lung is clear." A transfusion of 500 cc. was given. The patient's temperature became normal on the third day and did not rise again.

The discharge note made by Dr. Webb, on November 10, stated: "Patient was brought in suffering from gunshot wounds of the chest through the lungs, much hemorrhage took place. A blood transfusion was done. He recovered somewhat rapidly and was apparently well on discharge."

*Comment*—The striking feature in this case was the absence of hemothorax on the morning following the injury. There was a marked hemothorax one hour after the injury, but this leaked out. The course was unusually smooth, while the patient was in the hospital, and the condition cleared up rapidly. He was given a transfusion on the morning following his entry to the hospital, but the red blood cell count indicates that this was not urgently necessary. The fact that he had eliminated

*Laboratory Observations*

Date	Red Blood Cells	Hemo- globin, per Cent	White Blood Cells
November 29	3,540,000	60	7,200
November 30	3,600,000	60	11,800
November 31	4,200,000	70	6,100 } (two counts 5,900 } made)

the hemothorax and that blood was visible on the dressings gave rise to the belief that he had had an unusual amount of hemorrhage, and a transfusion was therefore given for safety. After the first day the temperature was never above 100 F.

By thus allowing the blood to escape slowly from the pleural cavity, the formation of an extensive hemothorax is prevented. This procedure was used as a routine measure in thirty-eight cases. None of the patients died. In six of the thirty-nine cases sufficient blood remained in the pleural cavity to justify aspiration.

The clinical course in patients who are kept free from the formation of an extensive hemothorax is smooth. They are almost free from fever, respirations are not labored, there is little shock and sweating, and the patient feels comfortable. In four cases, transfusions were made on account of loss of blood.

There has been a question in my mind from the beginning of this work as to whether it is wise to allow the escape of a hemothorax early after injury to the lung, since its presence is considered to be beneficial in reducing the hemorrhage from the lung. It seems logical to expect collapse of the lung to be beneficial in controlling hemor-

hage from it. However, there was no clinical evidence in the thirty-eight cases observed that the gradual and continuous escape of the blood from the pleural cavity increases the hemorrhage from the lung.

It has seemed to us that the gradual escape of the blood from the pleural cavity has certain desirable features that recommend it in preference to aspiration. In the first place, the leakage is continuous and slow while aspiration is done rapidly and at intervals. Aspiration produces a sudden expansion of the injured lung which would be expected to lead to hemorrhage. If the blood is allowed to leak out gradually as it escapes from the injured lung, no sudden change in the contour or size of the wound in the lung is brought about. Then, too, the escaping blood serves as an index to the amount of bleeding that is taking place. One can see it, 50 or 100 cc. of blood produces considerable soiling of the dressings. In contrast to this, much larger quantities may accumulate within the pleural cavity without their presence being noted. Frequent roentgenograms made with the chest in the upright position will reveal this blood. This, however, is difficult to accomplish. If the formation of a large hemothorax is prevented, the patient remains free from fever, he is comfortable and convalescence may be said to begin at once. With an extensive hemothorax even if sterile, the patient is usually sick and often has a temperature reaching 103 F. Finally the presence of a hemothorax is conducive to the establishment of an empyema. It should not be allowed to remain.<sup>13</sup>

#### RESULTS

Of the 162 cases reported here, 47 were stab wounds, and 115 gunshot wounds, of the chest. Seven of the cases of stab wound proved fatal, but the cause of death was associated stab wounds of the abdomen in 5 cases and immediate hemorrhage from the heart in 2 cases. No patient died of injury to the lung. Hemothorax occurred in 42 of the 47 cases. Two patients were operated on for ligation of the intercostal artery. The pleural cavity was not explored in either of these cases.

In the 115 cases of gunshot wounds of the chest, only 5 patients died when the pleural cavity only was entered by the bullet. Two of these died immediately of hemorrhage, and 3 died later as a result of infection of the pleural cavity and injured lung. A total of 27 of the 115 patients died. Twenty-two of these cases were complicated by associated wounds of the abdomen, spinal cord and skull. It is evident that patients with ordinary bullet wounds of the chest usually survive unless there are associated wounds which cause death.

<sup>13</sup> Allen, D. S. The Etiology of Empyema, *Surg. Gynec. Obst.* 45:23, 1927.

One of these patients died from associated injury of the left ventricle. This was correctly diagnosed and the mediastinum was immediately explored. The apex of the heart was found to have been shattered by the bullet to such an extent that it was impossible to check the hemorrhage.

Bullets were removed from 21 of the 115 patients with gunshot wounds. In 15 cases the bullets were embedded in the wall of the chest and could be removed without disturbance of the lung. In 6 cases the bullets were removed from the lung, but in no instance before two weeks had elapsed after the injury.

#### COMMENT

The treatment for gunshot and stab wounds of the pleural cavity has been directed, in the main toward removal or prevention of the formation of a hemothorax. It was not found necessary to operate immediately on the lung in a single instance. Only 7 of the 135 patients died who had penetrating wounds involving the chest only. Three of these died from hemorrhage from the heart. This low mortality rate in patients with simple stab and gunshot wounds of the pleural cavity indicates that it is seldom necessary to explore the chest in such cases.

The methods employed to deal with the hemothorax were simple aspiration, aspiration and immediate replacement of the aspirated blood by air, and, in thirty-eight cases, allowing the blood to leak out of the closed wound in the wall of the chest. In two of the latter thirty-eight cases, air was injected into the pleural cavity to allow for collapse of the lung, following this, the patient was placed with the closed wound down. The hemothorax gradually leaked out. This method of dealing with a hemothorax seems to be as logical as aspiration and the simultaneous introduction of air for replacement.

I wish to emphasize the fact that the commonest wounds of the chest, as they are met with in civil life, differ in type from the extensive wounds met with during the World War. Those occurring in civil life are usually the result of pistol bullets and stabbing with a knife. They seldom require surgical exploration of the pleural cavity.

#### ABSTRACT OF DISCUSSION

DR. A. T. BAZIN, Montreal, Canada. I was very much interested in Dr. Allen's presentation, particularly in that which is new to me—the ability of getting rid of a hemothorax by placing the patient on the wounded side. Collected blood in the pleural cavity clots slowly. Later it liquefies and aspiration of it can be maintained for a considerable period of time.

He has dealt with the most benign type of wound of the chest, gunshot wound. I think that Duval developed the radical treatment more for ragged wounds, shell wounds with wide open gaping wounds in the chest wall. In my first two years of war service I was in the field ambulance. We learned and in fact later were



ordered, to close these gaping wounds immediately with anything. The patient's condition immediately improved. Large doses of morphine were given frequently, and the patient was kept in a sitting position until he could be moved. My last year of service was at the base hospital, where there was a fairly large hut in which wounds of the chest were treated. There we met with cases of hematoma with gunshot wound.

There is one point that I should like to emphasize. As Dr. Allen suggests, if the cases are seen late, a hemothorax will not leak out after the wound is more or less sealed over. Something has to be done with the hemothorax. They can be classified as large and small. A small hemothorax, no broader than the hand may be let alone, with the patient sitting up, and no evil results will happen. I used to aspirate the large hemothorax.

Another classification is noninfected and infected hemothorax. We found, by collaboration with our pathologist, Laurence Rhea, that we could anticipate the infection of the hemothorax and deal with it accordingly. In routine aspirations every second day, cultures were made of the aspirated material, the fluid was spread out on a plate and little portions of clot could be picked out. These were crushed under a cover slip and stained, and occasionally one would find in those little pieces of clot definite colonies of organisms. As soon as that was discovered, the case was ready for operation, thoracotomy, thorough cleansing of the hemothorax and complete closure in layers, an airtight closure, with subsequent repeated aspirations. Under such treatment massive empyema or any severe infection in the pleural cavity was avoided. Getting rid of the residuum of clot, which is an excellent culture medium for the organisms, produced a comparatively mild infection of the pleural membranes.

DR. D. C. ELKINS, Atlanta, Ga. During the last year in Atlanta I had ninety-six cases of penetrative wounds of the chest, all occurring in Negroes. The great majority of them were due to ice pick wounds, a few to razor wounds and the rest to gunshot wounds. Of the ninety-six patients, eight died—seven of them within twelve hours—of extensive lesions, usually complicated by gunshot wounds of the abdomen, spinal cord, bladder or brain. In three of the eighty-nine patients who lived, empyema developed, one of these died of a staphylococcic septicemia, and in the other two patients chronic empyema developed that was exceedingly difficult to clear up.

Our method of treatment was to give all of the patients large amounts of morphine, to close the external wound when they were "sucking" and to begin the aspiration on the third to the fifth day, it was our opinion that if the fluid was left alone that long, it would compress the lung, as Dr. Lihenthal said and prevent further bleeding, and that after that time there would probably be no bleeding after the aspiration.

I was much interested in what was said in regard to placing these patients on the side for drainage. I shall certainly try it.

DR. C. D. LOCKWOOD, Pasadena, Calif. I think that this article of Dr. Allen's is timely, not only from the point of view of gunshot wounds, but from that of the number of crushed chests that are seen in automobile accidents and particularly in airplane accidents.

I agree more or less with what Dr. Bazin and Dr. Lihenthal said in regard to the treatment in some of these cases. In the group of cases in which Duval undoubtedly first started his operation the patient otherwise died in advanced operating centers or in the casualty clearing station and was never sent to the base area at all. These patients had a wide open chest with an extensive hemo-

thorax, the opening of which was so wide that it could not be kept closed by suture or by adhesive plaster. The patient died within an average of from twenty-four to forty-eight hours. Those who reached the casualty clearing station alive were dead within usually forty-eight hours. This occurred until July, 1916. For a year and a half I had made a practice of observing cases of this type every day and consigning a certain portion of them to a moribund ward. The patients were given morphine and left to die. Beginning with the last week of July the mortality of 80 per cent in that group was changed to 33 per cent for twelve months out of the year.

That type of procedure applied to cases of a wide open chest in which there was no hope of saving the patients except by radical measures. In these gunshot wounds of the chest one has to keep in mind one or two of the problems of which Dr Allen spoke, particularly that of whether or not the wound is a ragged type that might have carried some clothing into the chest. In this case an infected hemopneumothorax would occur, on the other hand if it is a clean type of bullet wound, with a small hemothorax, and if the patient is getting along fairly comfortably, one should wait for some time. We have made the rule, however, that these patients should be looked on as emergency cases day and night, that the physician in charge of that work should be called immediately when the patient's condition seems to require it, and that he should constantly observe the patient for the first six to eight hours. When the patient does not improve gradually, we give him a transfusion and get ready for the operation. We would not aspirate the chest under any conditions at that time, but we might attempt to put more air into the chest as Dr Lilienthal has said.

For five years I have been taking a rather active interest in the flying corps in my country, and we have rather active clubs there at the present time. There is a rule that all flyers carry a small emergency kit, so that if a flyer crashes and has an open wound in the chest, it can be sewn, if possible, or covered with adhesive tape. Besides this they are provided with the ordinary first field dressing used during the war and with a small ampule of morphine tablets to take by mouth. By tiding them over with morphine and by closing the opening in the chest we hope to prevent the mortality that occurs in these cases in the first half hour. If the patient reaches the hospital, even though he has a badly staved-in chest we may be able to do something for him.

We deal with these cases as we did during the war. We watch the patients closely, and if they are not holding their own and have a large hemothorax, we prepare to operate on the chest. I think that one must follow the same procedure with gunshot wounds if the patients are not holding their own at the end of about six hours. If they have a clean bullet wound, I think that they ought to be let alone. They ought to be given the benefit of any doubt, however, and operated on rather than be let alone.

DR F T LORD, Boston. I should like to suggest in addition that the cultures be made under anaerobic as well as aerobic conditions.

DR H BRUNN, San Francisco. I believe that all are agreed that the conservative or expectant method of treatment is, in general, the preferable course to follow in the treatment for penetrating wounds of the chest. It has been my experience, however, that this method of treatment does not answer the question for all cases. When death occurs the question arises as to whether or not more active measures taken earlier would not have been the better policy. I feel, therefore, that careful observations must be made on every penetrating wound in its earlier stages in order to decide if the hemorrhage is uncontrolled and if a radical procedure is indicated.

In looking over statistics at the San Francisco Hospital for a period of ten years and following up some of the cases, we discovered that while patients were discharged as cured they were left disabled because of inability to resume their usual occupations. This was usually the result of adhesions which caused a great diminution in their vital capacity.

As a result of these observations we adopted in our conservative measures a certain line of treatment. As soon as fluid collects in the pleural cavity it is withdrawn and an equal quantity of air is put in with a pneumothorax machine and the pressure read. We do not remove fluid without replacing with air. By this means we are enabled to remove the fluid early without setting up the hemorrhage afresh by the release of pressure. We also believe that fluid in the pleural cavity is defibrinated by the churning action of respiration and that this deposit of fibrin early covers the parietal and visceral pleura and quickly becomes organized, fixing the lung in an unnatural position.

Our policy, therefore, is to treat penetrating wounds conservatively, watching the case carefully for the first three or four days for hemorrhage and infection and not hesitating on early indications for radical measures. I believe the withdrawal of fluid from the chest and the replacement of air to be a great advantage in the conservative treatment in such cases.

DR C. M. VAN ALLEN, New Haven, Conn. On the subject of coagulation of the blood that is accumulating in the chest in these cases, I should like to ask Dr. Allen if he has any explanation for the failure of coagulation of the blood as it lies in the pleura. I should like to add an observation of my own in that regard.

Some time before the present meeting, a patient was admitted to the hospital who had shot himself with a revolver in the left side of the chest. On admission, he showed a large hemothorax. Expectant treatment was used, and two weeks later he seemed to be fully recovered except that he had a large mass of blood in the pleural cavity. We undertook aspiration of the blood. The blood flowed through the needle easily, and we took out about 1,000 cc the first time, stopping simply because we felt that we ought not to take out more than that at one time. The blood was still fluid at the end of two weeks. When it went into the bottle, it clotted within a minute or so, so that on being shaken, it was completely jelled.

In this case the blood that stayed in the chest for two weeks clotted immediately on being eliminated from the chest, and apparently in that case, at least, we would have been misled if we had taken the clotting as a sign of fresh bleeding.

DR ALLEN. In the consideration of this series of cases, I did not mention the treatment for larger wounds of the chest wall and lung, as there were none of that type. Duval and others advocated thorough exploration of the chest, repair of the lung, and removal of the large missiles in this type of case. In cases with bullet wounds that produced small wounds of the chest wall and lung, it was not found necessary to explore. This distinction is important.

I agree with Dr. Lihenthal that one should not attempt to aspirate the hemothorax immediately after it has formed. It seems logical to suppose that aspiration of the hemothorax at this time would increase the hemorrhage from the wound in the lung. I have been unable to find definite proof, however, that gradual aspiration of the blood would increase the hemorrhage. I think that one may safely turn the patient so that the closed wound is dependent and thus allow the hemothorax to leak out slowly.

In regard to the failure of the blood to clot within the pleural cavity, Henry and Elliot in a series of cases during the war determined that the blood con

tained in a hemothorax was really defibrinated blood. An exudate from the pleura often contaminated the blood and produced the clotting when all the fluid was withdrawn from the pleural cavity. They stated that the blood contains no fibrinogen. This does not seem to me to hold in all cases. In certain cases observed during the war all the blood contained within the pleural cavity was found to be liquid, and there were no masses of fibrin. I do not know how to explain this on the basis of immediate clotting and subsequent defibrination.

DR P. N. CORLIOS, New York. The penetrating wounds of the thoracic cavity due to small bullets should be distinguished from the large openings of the thoracic cavity caused by a bayonet, a knife, fragments of shells or trench torpedoes, as were those seen during the World War. In these cases, because of the wide opening of the pleural cavity and the collapse of one lung, asphyxia was (in the absence of great hemorrhage) the most immediate danger. Survival or immediate death depended on the resistance offered by the mediastinum. An elastic and yielding mediastinum that allowed serious interference with function of the other lung was incompatible with the survival of the wounded. However, during my service in Verdun, France, I saw a number of cases of unbelievably wide openings of the chest in which I consider that the survival during transportation from the battlefield to the advance ambulance was due to the obduration of the wound by the clothes of the wounded or to the tight dressing applied to the wound. In these cases the only thing to do was to trim the wound rapidly, to stop the hemorrhage by tying the bleeding points, even if it were on the lung tissue, and to close the cavity. The after-treatment depended on the behavior of the wound. Generally no evacuation of the fluid accumulating in the thoracic cavity was done before the third or fourth day, unless vitally indicated. After that time, since, as a rule, infection would set in, the fluid was tapped and as much as possible gradually aspirated. In these cases the infections were usually anaerobic. If the patient survived the first three to five days, empyema generally set in, the management of which was easier than that of anaerobic infection. Besides these cases, however, I saw, some marvelous recoveries with practically primary healing.

Another class of wounds that I should like to mention were wounds of the lung caused by small splinters of shell or trench torpedoes that exploded a short distance from the patient and therefore possessed great momentum. In these wounds no pneumothorax or even hemothorax of any importance was present. They appeared to be slight injuries. Two or three days later, however, symptoms of pneumonitis would develop on the affected side, and the patient would soon die with signs of severe general toxemia. Postmortem examination would disclose signs of deep disorganization of the affected parenchyma and gas gangrene rapidly spreading around a foreign body that sometimes did not exceed the size of a small pea or lentil.

I mention these cases because they show the extreme variability of the different penetrating wounds of the thoracic cavity and because of the possibility of standardized therapeutic methods for them. I firmly believe that in the second variety of cases, after the localization of the foreign body, the best method is to perform a thoracotomy and trim out the wounded lung parenchyma, in other words, to apply to the lung the same principles of preventive debridement that gave such brilliant results in the treatment for wounds of the knee joints and of the soft tissue.

On the other hand, I should be extremely conservative in the treatment of bullet wounds, although I agree with Dr. Allen that the early evacuation of

hemothorax, made with caution, is an excellent measure. It often prevents the development of secondary infection and hastens recovery.

DR. HOWARD LILIENTHAL, New York. I have had some experience with gunshot wounds of the chest and other wounds, too. There are some things that Dr. Allen has said with which I cannot quite agree. I do agree with Dr. Allen if he is sure of the kind of injury that the patient has had, but this is very difficult. A patient may die of hemorrhage from an intercostal artery that has been wounded. Nonintervention in such a case would be serious, resulting in death from hemorrhage into the chest. Or there may be fatal bleeding outside which, in the cases such as those illustrated by Dr. Allen, might, of course, be mistaken for intrathoracic bleeding with external leakage. The presence of clot in the recently exuded blood is a very important sign and calls for immediate intervention.

Was the percentage of hemoglobin 60 immediately after the hemorrhage?

DR. DUFF ALLEN. The next day.

DR. HOWARD LILIENTHAL. That is perfectly possible, but I could not conceive of a hemoglobin reading of 60 per cent immediately after the hemorrhage. The hemoglobin reading should then be just what it was before the man was injured.

Blood pressure readings are of the greatest importance in these cases in deciding on operation.

I do not think that hemothorax should be aspirated, because the intrapleural tension tends to hold the lung in compression and maintain closure of the wound in the lung if there is one. On aspiration the lung is expanded, the pulmonary wound reopens, and the hemorrhage begins again. I should rather use artificial pneumothorax than aspiration in cases of this kind.

# ETIOLOGY OF PRIMARY BRONCHIECTASIS<sup>4</sup>

DAVID T SMITH, M D

RAY BROOK, N Y

For the purposes of this paper bronchiectasis is considered primary when the ulceration and dilatation of the bronchial tree cannot be ascribed to any preceding or underlying pathologic process in the lungs or bronchi. Thus I have excluded from consideration all lesions occurring in the course of tuberculosis both the true tuberculous ulcerations of the bronchial wall and the more common forms of bronchial dilatation seen in chronic fibroid phthisis, in lungs collapsed by artificial pneumothorax or by thoracoplasty, and in old atelectatic lungs. The latter lesions are usually mere mechanical dilatations due to the stretching and distortion of the bronchi by fibrous tissue, and, on section, the bronchial wall is seen to be intact, in contrast to primary bronchiectasis in which ulceration and destruction of the elastic tissue are conspicuous. The definition also excludes bronchiectasis secondary to stricture of the bronchus due to aneurysm, neoplasm or foreign body, as well as dilatations caused by fibrous contractions in pleurisy, cirrhosis of the lung and unresolved pneumonia. I shall disregard the relatively rare cases of congenital cystic bronchiectasis first described by Grawitz<sup>1</sup> and the more common acute dilatations of the bronchioles following infection with *B influenzae*. This leaves for consideration as primary or essential bronchiectasis only those cases of nontuberculous ulceration and dilatations of the larger bronchi characterized by a chronic course, distressing cough, and large amounts of sputum which may be very foul.

Primary bronchiectasis is analogous to aneurysm in many respects<sup>2</sup>. Both arteries and bronchi are hollow muscular tubes, the main strength of which is derived from the dense sheet of elastic tissue in their walls<sup>3</sup>. Arteries cannot dilate until the integrity of the elastic tissue layer is destroyed by the action of *Spirochaeta pallida* permitting the formation of sacculated, cylindric or fusiform aneurysms. Similarly,

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<sup>4</sup> From the New York State Hospital for Incipient Tuberculosis.

<sup>1</sup> Grawitz, P. Ueber angeborene Bronchiectasie, Virchows Arch f path Anat **82** 217, 1880.

<sup>2</sup> This similarity between aneurysm and bronchiectasis was suggested to me by Dr H A Bray, Superintendent of the New York State Hospital for Incipient Tuberculosis.

<sup>3</sup> Macklin, C C. Functional Aspects of Bronchial Muscle and Elastic Tissue, Arch Surg **19** 1212 (Dec) 1929.

in my opinion, the bronchi present the sacculated, cylindric or fusiform dilatations characteristic of primary bronchiectasis only after the elastic tissue fibers have been weakened and ruptured by the action of an anaerobic group of organisms which includes among its members *Treponema microdentium* and *Treponema macrodentium*.

In previous contributions<sup>4</sup> I have shown that Vincent's angina, pulmonary gangrene and pulmonary abscess are all due to the symbiotic action of the group of anaerobes found in pyorrhea alveolaris, this group includes *T. microdentium*, *T. macrodentium*, *S. Vincenti*, *S. buccalis*, fusiform bacilli, vibrios and cocci. In this paper I propose to present clinical and experimental evidence to show that the essential lesion of primary bronchiectasis, i. e., the destruction of the elastic coat of the bronchus, is caused by focal necrosis due to infection with this same fusospirochetal group of anaerobic organisms. These organisms are constantly present in the sputum of active cases of bronchiectasis and can be demonstrated in properly stained sections deep in the tissues of the diseased bronchi. With these anaerobic organisms bronchial disease may be produced in rabbits which is comparable to bronchiectasis in man.

Many observers have noted the presence of spirochetes and other organisms of the mouth in the sputum from cases of bronchiectasis (Leyden and Jaffe,<sup>5</sup> Rona,<sup>6</sup> Buday,<sup>7</sup> Nolf,<sup>8</sup> Pilot and Davis,<sup>9</sup> Kline and Berger,<sup>10</sup> and Smith<sup>11</sup>)

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4 Smith, D. T. Experimental Aspiratory Abscess, Arch Surg **14** 231 (Jan) 1927, Bronchopulmonary Spirochetosis, Am Rev Tuberc **15** 352 1927, Fusospirochetal Disease of the Lungs, ibid **16** 584, 1927, Fusospirochetal Diseases of the Lungs, Tubercle **9** 420, 1928, Relation of Vincent's Angina to Fusospirochetal Diseases of the Lungs, J A M A **94** 23 (Jan 4) 1930, Fusospirochetal Disease of the Lungs Produced with Cultures from Vincent's Angina, J Infect Dis **46** 303 (April) 1930.

5 Leyden and Jaffe. Ueber putride (fotide) sputa nebst einigen Bemerkungen über Lungenbrand und putride Bronchitis, Deutsches Arch f klin Med **2** 488, 1867.

6 Rona. Zur Aetiologie und Pathogenese der Plaut-Vincentischen angina, Arch f Dermat u Syph **74** 171, 1905.

7 Buday. Histologische Untersuchungen über die Entstehungsweise der Lungengangran, Beitr z path Anat u z allg Path **48** 70, 1910.

8 Nolf, P. Fetid Spuillar Bronchitis and Pulmonary Gangrene, Arch Int Med **25** 429 (April) 1920.

9 Pilot, I., and Davis, D. J. Studies in Fusiform Bacilli and Spirochetes—Their Rôle in Pulmonary Abscess, Gangrene and Bronchiectasis, Arch Int Med **34** 313 (Sept) 1924.

10 Kline, B. S., and Berger, S. S. Spirochetal Pulmonary Gangrene Treated with Arsphenamins, J A M A **85** 1452 (Nov 7) 1925.

11 Smith, D. T. (footnote 4, references 1, 2 and 3)

In demonstrating the spirochetes and fusiform bacilli in the sputum from cases of bronchiectasis, special care in the selection of the specimen for examination is important. The residual sputum from the depth of the lungs is the most desirable, so I try to obtain the last purulent material that is raised after a coughing spell in the morning, or better still the last material raised following postural drainage. In many cases the residual sputum will contain spirochetes and fusiform bacilli when chance specimens taken during the day or even the first portion raised during postural drainage fails to show these anaerobic

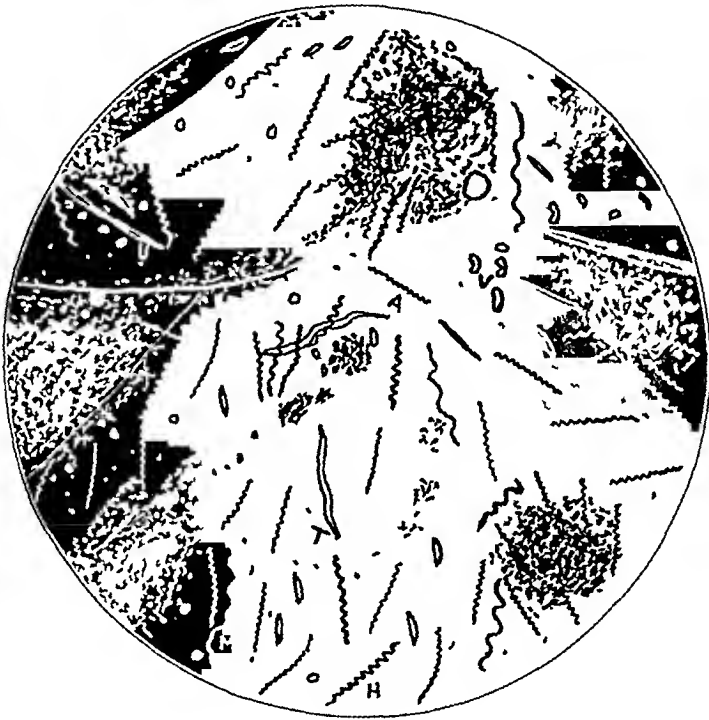


Fig 1—Drawing made from a dark-field preparation of a granule from the sputum of a patient with chronic bronchiectasis. *A* indicates *T. microdentium*, *H*, *T. macrodentium*, *M*, *S. Vincenti*, *T*, *S. buccalis*, *U*, large fusiform bacillus, *V*, vibrio.

organisms. In other cases spirochetes and fusiform bacilli are found in the sputum only when the patient is having an increase in symptoms. The fusiform bacilli are best stained by either Sterling's gentian-violet or carbol-gentian-violet. The thicker spirochetes *S. buccalis* and *S. Vincenti*, may also be seen with the gentian-violet stain, but the smaller spirochetes, *T. macrodentium* and *T. microdentium*, are generally not stained by this method. They have to be studied by either the Fontana stain or preferably the dark-field apparatus (fig 1). Smears for the Fontana stain and wet preparations for dark-field



examination have to be made exceedingly thin, otherwise the delicate spirochetes are all hidden by debris

During the past five years I have had the opportunity of studying 100 cases of nontuberculous bronchial disease. Bronchiectasis was demonstrated in 60 cases by the injection of iodized poppy seed oil 40 per cent. Spirochetes, fusiform bacilli, vibrios and cocci were found in 49 or 82 per cent and in every one of the 49 cases the iodized oil revealed the characteristic picture of bronchiectasis. Among the 51 cases in which spirochetes and fusiform bacilli were not found in the sputum, 40 showed essentially normal bronchi by the injection of iodized oil, while 11 had dilated bronchi. The bronchial disease in the latter group might have been caused by some other type of organism or the characteristic anaerobes might have disappeared before the sputum was examined. A spontaneous cure accounts for 3 of these 11 cases since at the time of the injection of iodized oil there was no cough or expectoration, although there was a history of

*Correlation of Bacteriology and Iodized Oil*

Iodized poppy seed oil 40% in 100 cases of bronchial disease	{	80+	{	49 — Spirochetes and fusiform bacilli
				11 — No spirochetes or fusiform bacilli
		10—		No spirochetes or fusiform bacilli

foul sputum present over a period of years. In two other cases I have observed the spontaneous disappearance of the fusospirochetal organisms when the patients were treated by postural drainage. In a number of patients treated with both postural drainage and repeated courses of neoarsphenamine or sulpharsphenamine the spirochetes disappeared first, the fusiform bacilli and the vibrios next, and the cocci last. Indeed, the cocci often persist for years after the other organisms are gone and after the patient is in excellent physical condition.

Bronchiectasis may begin in any one of three ways. A membranous exudate may form on the surface of the bronchial wall similar to the membrane of Vincent's angina, and ulceration take place beneath this covering. Chevalier Jackson studied two such cases with the bronchoscope.<sup>12</sup> More commonly bronchopneumonia is produced by the anaerobic organisms in which certain of the terminal bronchi are filled solidly with exudate. These organisms then invade the bronchial wall, destroying the elastic tissue support and produce bronchiectasis. In the third type, bronchiectasis develops in the bronchi in which a

<sup>12</sup> Jackson, C. Ulcerative Bronchitis Due to Vincent's Organisms. J. A. M. A. 83: 1845 (Dec 6) 1924.

lung abscess is draining. The constant contact of the fusospirochetal material with the bronchus finally results in infection and ulceration. This process is illustrated in figure 2. Some of the bronchial mucosa cells still show cilia, but the spirochetes followed by fusiform bacilli, vibrios and cocci have penetrated deeply into the bronchial wall. To the left of the area illustrated, the bronchial mucosa was already destroyed, and the organisms were penetrating the elastic tissue layer.

The next stage in the process of bronchial ulceration is shown in figures 3 and 4. Here a bronchial lesion hardly larger than the head of a pin has already cut entirely through and destroyed the integrity

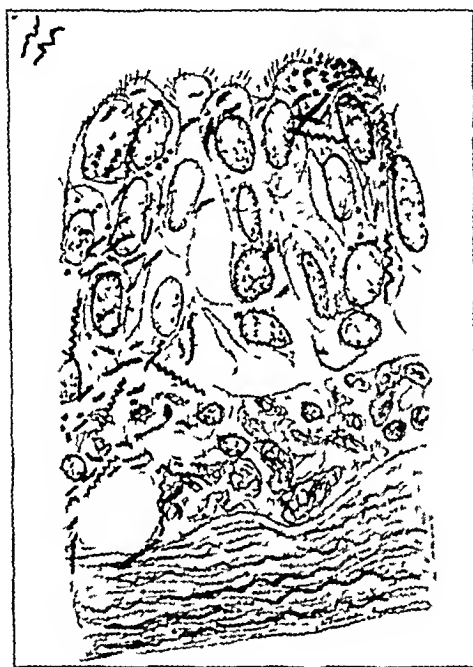


Fig 2—Drawing made from the bronchus of a child with a pulmonary abscess. The sputum from the abscess drained through this bronchus. Fusiform bacilli and spirochetes are seen invading the wall of the bronchus. Levaditi stain.

of the elastic tissue layer. The size, distribution and location of the lesions determine whether the resulting dilatation is fusiform, cylindrical or sacculated (Fig 5).

Sections from twelve cases of bronchiectasis have been examined for fusiform bacilli and spirochetes. The tissues were stained by the method introduced by Levaditi for the demonstration of *Spirochaeta pallida*. Spirochetes and fusiform bacilli were found in eight of twelve cases. The ones that did not show the organisms were old chronic cases of years' duration. Dr Leroy U Gardner of the Saranac Lake Laboratory gave me the opportunity to examine sections from

six other cases which were stained with Goodpasture stain following fixation in Zenker's solution. Spirochetes cannot be demonstrated by this method but fusiform bacilli were found in four of the six cases. Buday<sup>7</sup> and Pilot, Davis and Shapiro<sup>11</sup> have also demonstrated spirochetes and fusiform bacilli in the bronchial wall tissue from cases of bronchiectasis.

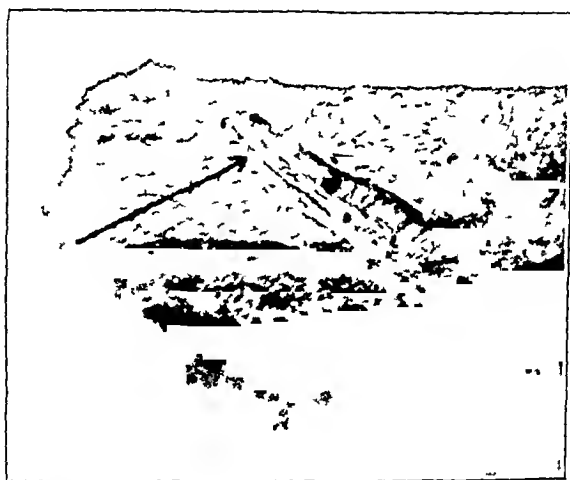


Fig 3—Photograph of a small bronchial ulcer. Smears from the lesion showed spirochetes, fusiform bacilli and cocci.



Fig 4—Photomicrograph of a section of the bronchial ulcer shown in figure 3. The mucosa can be seen covering a portion of the surface. The elastic tissue and muscular layers are completely destroyed in the central portion,  $\times 150$ .

#### EXPERIMENTS

In a previous study of experimental pulmonary disease in guinea-pigs caused by aspiration of fusospirochetal material, I observed ulcerations.

<sup>11</sup> Pilot, I., Davis, D. J., and Shapiro, I. J. Studies of Fusiform Bacilli and Spirochetes, *Am Rev Tuberc* 8:249, 1923.

tions of the bronchi which were not of sufficient extent to be called bronchiectasis<sup>14</sup> Allen<sup>15</sup> and Harkavy<sup>16</sup> observed similar lesions in the smaller bronchi of dogs infected with fusospirochetal material Weidlein and Herrmann<sup>17</sup> obtained definite ulceration and dilatation of the bronchial wall in one dog by fastening cotton soaked with fusospirochetal material in the bronchi

In the following experiments I attempted to produce bronchiectasis in rabbits by the simple aspiration method, since the clinical data suggest that this is the route by which the anaerobic organisms from pyorrhea alveolaris reach the bronchi Material from three different sources was used In the first experiment, scrapings from about the

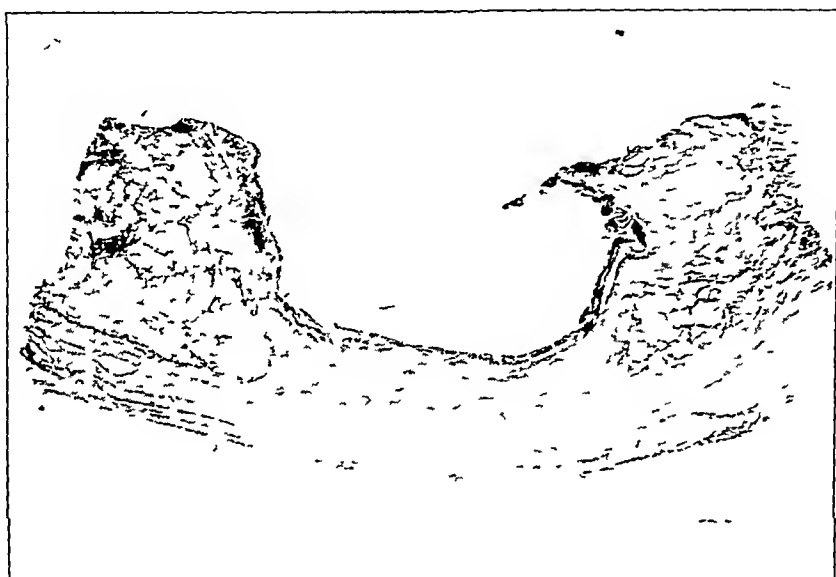


Fig 5—Photomicrograph of a section from an old case of bronchiectasis The elastic tissue and muscular layers are largely destroyed and are surrounded by a dense layer of fibrous tissue,  $\times 10$

teeth of patients with moderately severe pyorrhea was employed For the second experiment sputum from a case of acute fusospirochetal bronchitis was used Sputum from a case of pulmonary abscess was utilized in the third experiment In the fourth experiment control inoculations were made with pure cultures of (1) *Staphylococcus*

14 Smith, D T (footnote 4, reference 1)

15 Allen, D S Etiology of Abscess of the Lung, Arch Surg **16** 179 (Jan) 1928

16 Harkavy, J The Pathogenesis of Aspiratory Abscess of the Lung Arch Int Med **43** 767 (June) 1929

17 Weidlein I F, and Herrmann L G Abscess of the Lung Experimental Study in Chronicity J A M A **91** 850 (Sept 22) 1928

*aureus*, (2) aerobic hemolytic streptococci, (3) anaerobic hemolytic streptococci, (4) green-producing streptococci, (5) an anaerobic streptothrix, (6) Friedlander's bacillus and (7) influenza bacillus. All of these organisms were isolated from the sputum of cases of nontuberculous pulmonary disease.

*Experiment 1*—A guinea-pig was inoculated in the groin with 0.5 cc of pyorrhea material. After eight days the animal developed a large abscess containing thin foul-smelling purulent material which showed on examination large numbers of spirochetes, fusiform bacilli, vibrios and cocci. One-fourth cubic centimeter of this material was introduced into the trachea of each of six rabbits. The rabbits were anesthetized, the trachea dissected out and elevated to the surface, a 14 gage needle introduced into the trachea, and the material was slowly introduced with a tuberculin syringe. The head of the animal was elevated and the



Fig 6—Roentgenogram of the chest of a rabbit. The lungs show a sacculated dilatation by iodized oil.

body rotated so that the purulent material would flow into the left lower lobe. Four days later roentgenograms of the rabbits were made, and all were found to have a shadow in the lower part of the left lung. The same day a dose of (15 mg per kilogram) sulpharsphenamine was injected intravenously. The sulpharsphenamine was given with the idea that some of the spirochetes would be killed, and the progress of the disease retarded, so that the ulceration might be confined to the bronchi rather than invade the whole lung as in abscess or gangrene.

One animal died on the fifth day with extensive gangrene of the left lung. One died on the sixth and two on the eighth day with abscess of the left lung complicated by empyema. One rabbit, which lived for fifteen days, on post-mortem injection of iodized oil presented the picture of bronchiectasis (fig 6). At necropsy, there were extensive ulceration and destruction of the bronchial wall, and the characteristic fusospirochetal combination of organisms were demonstrated in smears made from the lesion. The sixth rabbit made a complete recovery.

*Experiment 2*—A guinea-pig was inoculated in the groin with sputum from a case of acute bloody bronchitis, which contained large numbers of spirochetes, fusiform bacilli, vibrios and cocci. An abscess appeared in six days, and pus from this, in amounts of 0.25 cc was injected into the trachea of six rabbits as in experiment 1. Roentgenograms showed shadows in the left lung of all the animals on the fourth day when they were given sulpharsphenamine intravenously (15 mg per kilogram). A second dose of sulpharsphenamine was given two days later.

Two rabbits died on the seventh day with pulmonary gangrene, one died on the ninth day and one on the twelfth day with abscess and empyema. The last two rabbits died on the sixteenth and twentieth days, respectively, and bronchiectasis was demonstrated by both postmortem injection of iodized oil and



Fig 7—Photomicrograph of multiple dilatations of the bronchi of a rabbit infected with fusospirochetal material,  $\times 10$

necropsy (fig 7). Fusiform bacilli, vibrios and cocci were found in smears from the lesions, but no spirochetes. The spirochetes were probably killed by the arsenic therapy.

*Experiment 3*—In this experiment an attempt was made to increase the resistance of the rabbit by intravenous injections of heat-killed abscess material. Sputum, containing spirochetes, fusiform bacilli, vibrios and cocci from a case of pulmonary abscess was injected into the groin of a guinea-pig. Some of the purulent material from the experimental abscess was heated in a water bath of 60 C for one hour, and then cultivated anaerobically to demonstrate the sterility. Ten rabbits received in the ear vein 0.25 cc of this material in 1 cc of saline solution. A second and third injection were given at weekly intervals. A week after the last injection, 0.25 cc of the living fusospirochetal material which had been kept alive by transfer from pig to pig at eight to ten day intervals, was

introduced into the trachea as in experiment 1. Roentgenograms of the chest, made four days later, showed some evidence of disease in eight of the ten animals. Either the infecting organisms had lost some of their virulence, or the rabbits had acquired a considerable degree of resistance, for the animals all recovered within two weeks.

The ten rabbits were then reinoculated intratracheally with 0.5 cc of fusospirochetal material. On the fourth day after inoculation, roentgenograms of all the animals showed extensive infection of the left lung. On the same day, each rabbit was given a dose of sulpharsphenamine intravenously (15 mg per kilogram). Two rabbits died of pulmonary gangrene on the fifth day and two others on the sixth day. The survivors were given another dose of sulpharsphenamine on the sixth day. Three other animals died of pulmonary abscess between the eighth and tenth days of the experiment.

The shadows in the surviving rabbits gradually cleared over a period of two months, as demonstrated by the roentgenograms. One animal recovered entirely. The other two presented bronchiectasis which could be demonstrated in the living rabbit with injection of iodized oil. The animals were killed, and the diagnosis confirmed at necropsy.

*Experiment 4*—As a control to the foregoing experiments each of two rabbits received intratracheally a saline suspension of one fourth of the total growth of a pure culture of *Staphylococcus aureus* from a blood agar slant, the total growth from two blood agar slants of a pure culture of an aerobic hemolytic streptococcus, the total growth from two blood agar slants of a pure culture of an anaerobic hemolytic streptococcus, the total growth from two blood agar slants of a pure culture of a green-producing streptococcus, total growth from a blood agar slant of a streptothrix, and the total growth from two blood agar slants of a pure culture of *B. influenzae*. Five rabbits received intratracheally one fourth of the contents of a blood agar slant of a pure culture of a Friedlander's bacillus.

On the fourth day all seventeen animals showed evidence of disease in the roentgenograms, but with the exception of three of the five that received the Friedlander's bacillus, all the rabbits had normal lungs at necropsy three weeks later. No permanent damage was produced in the bronchi by any of these seven types of organisms.

#### COMMENT

The influenza bacillus is present in a certain percentage of cases of bronchiectasis, and some authorities assume that it is the essential cause of the disease. During the last great epidemic, Opie, Freeman, Blake, Small and Rivers,<sup>18</sup> found influenza bacilli producing purulent bronchiectasis of the terminal bronchi in patients dying of postinfluenzal pneumonia. Later Blake and Cecil<sup>19</sup> demonstrated similar lesions in monkeys that had been infected with pure cultures of *B. influenzae*. It has, however, never been conclusively proved that *B. influenzae* can destroy the elastic tissue of the larger bronchi. Although

18 Opie, E. L., Freeman, A. W., Blake, F. G., Small, J. C., and Rivers, T. M. Pneumonia Following Influenza, *J. A. M. A.* **72**: 556 (Feb. 22) 1919.

19 Blake, F. G., and Cecil, R. L. Nine Studies on Experimental Pneumonia. *J. Exper. Med.* **32**: 691, 1920.

the work of Garvin, Lyall and Morita<sup>20</sup> shows that this organism can produce a chronic bronchitis with moderate dilatations of the bronchioles, I am not convinced that the influenza bacillus can initiate the type of bronchiectasis discussed in this paper.

On the basis of etiology, there is no sharp line of differentiation between pulmonary gangrene, pulmonary abscess and bronchiectasis. My experience confirms the opinion of Whittemore<sup>21</sup> that every case of bronchiectasis presents more or less involvement of the parenchyma. Exactly the same combination of anaerobic organisms that appears to be the cause of pyorrhea alveolaris is found in pulmonary gangrene, pulmonary abscess and bronchiectasis. In the first experiment recorded material from pyorrhea alveolaris was used in the second, sputum from a case of fusospirochetal bronchitis, and in the third, sputum from a case of pulmonary abscess. The same combination of anaerobic organisms was present in the material from the three sources and it was found that some rabbits in each group developed gangrene, some abscess and some bronchiectasis.

#### SUMMARY AND CONCLUSION

The essential lesion in primary bronchiectasis is a focal necrosis of the elastic tissue in the bronchial wall due to infection with the fusospirochetal group of anaerobic organisms. This fusospirochetal group, comprising *T. macrodentum*, *T. microdentum*, *S. Vincenti*, *S. buccalis*, fusiform bacilli, vibrios and cocci, are the same organisms that are found in pyorrhea alveolaris, Vincent's angina, pulmonary abscess and pulmonary gangrene.

These organisms have been seen in the sputum of forty-nine of sixty patients proved to have bronchiectasis by the iodized oil test.

Spirochetes and fusiform bacilli were found in sections of bronchial dilatations after staining by Levaditi's method in eight of twelve cases which came to necropsy. Fusiform bacilli were demonstrated in pathologic sections from four of an additional six cases of bronchiectasis after staining by Goodpasture's method.

In animal experiments, fusospirochetal material from varied sources (pyorrhea alveolaris, fusospirochetal bronchitis and pulmonary abscess) caused bronchiectasis as well as pulmonary abscess and pulmonary gangrene in rabbits.

<sup>20</sup> Garvin, A. H., Lyall, H. W. and Morita, M. Chronic Nontuberculous Lung Infection. *Am. Rev. Tuberc.* **1**: 16, 1917.

<sup>21</sup> Whittemore, W. The Treatment of Chronic Broncho-Pulmonary Suppurative Lesions Limited to One Lobe of the Lung. *New England J. Med.* **199**: 1213, 1928.



Control inoculations with pure cultures of (1) *Staphylococcus aureus*, (2) aerobic hemolytic streptococci, (3) anaerobic hemolytic streptococci, (4) green-producing streptococci, (5) anaerobic streptothrix, (6) Friedlander's bacilli and (7) influenza bacilli failed to produce damage to the bronchi.

The fusospirochetal group of organisms is probably the cause of primary bronchiectasis.

#### ABSTRACT OF DISCUSSION

DR F T LORD, Boston. Much credit is due Dr. Smith for his painstaking work in this difficult bacteriologic field. In both the postoperative group of patients with abscess of the lung and the group on which operation had not been performed, the disease arises so frequently apart from lobar or obvious bronchopneumonia as to suggest that it is not an accident of resolution but an independent condition. Ingress into the deeper parts of the respiratory tract of infected material from above is to be regarded as the chief cause of pulmonary abscess. It is largely as a result of Dr. Smith's investigations that increasing attention has been paid to spirochetes and fusiform bacilli as a cause of abscess of the lung. As he has pointed out, the bacterial flora of abscess is that of the tonsillar crypts and the teeth, and the same assortment of organisms, including spirochetes, fusiform bacilli, cocci and vibrios, obtains in postoperative and nonoperative abscess. Animal experiments suggest that not one organism alone is the cause, but that symbiosis is essential for the production of abscess. Bacterial association favorable to the multiplication of certain organisms in culture mediums has long been noted and may be necessary for the production of pulmonary abscess, but the necessity for the introduction of this principle and the inability to establish the presence of these organisms in all cases of abscess make it inadvisable to accept without question their etiologic relation with the disease. It may nevertheless be said that from his work certain cases of abscess and bronchiectasis are known probably to be due to these organisms.

Bronchiectasis, from a pathologic point of view, is uncommon and only rarely merits an independent position. It usually arises under conditions that make it desirable to regard it as a relatively unimportant complication in the course of a bronchopulmonary disturbance. The pathologic process in the lung is ordinarily much more important than the bronchial dilatation. Roentgenologic interpretations are largely responsible for the frequency and undue importance accorded this condition clinically, and it seems unfortunate that the term is so freely used.

DR CARL A HEDBLUM, Chicago. I was particularly interested in Dr. Smith's paper because of the light it throws on the etiology of bronchiectasis. From clinical studies we recognize a variety of causes for this condition, the most important of which are the acute infectious diseases of childhood, bronchopneumonia occurring at any age and the various conditions that result in permanent atelectasis and those that produce an extensive fibrosis of the lung, including fibroid phthisis. In a considerable proportion of cases the cause cannot be determined. A considerable proportion of these cases of indeterminate etiology are probably congenital. Sauerbruch has expressed the opinion that most of the cases of left-sided involvement are congenital. I am inclined to the opinion that aspiration of such organisms as Dr. Smith described may be the determining factor in a large proportion of the cases of indeterminate etiology.

With regard to pathologic changes, I cannot quite agree with my good friend, Dr Lord. Necropsy in cases of long duration and in patients who died of complications would naturally be expected to show pulmonary involvement in large proportion. We see many patients, however, who presumably have had bronchiectasis for many years, who have no outstanding symptoms except cough and sputum and who remain in fairly good health. Physical examination shows only a few rales, and roentgenograms show little or no evidence of pathologic processes in the parenchyma of the lung. Pathologists usually do not see these cases until complications have developed.

One of the practical conclusions that we may draw from Dr Smith's investigation is the importance of preoperative prophylaxis of the mouth and throat and of treatment with arsphenamine in cases in which we have reason to believe that spirochetes are among the infective organisms.

DR C M VAN ALLEN, New Haven, Conn. Dr Smith is to be congratulated on his work, because, beginning with his paper presented two or three years ago before the Society, it represents the main work that has fixed this spirochetal disease as one of the main factors in chronic suppurative diseases of the lung. Following that paper his work has been corroborated, of course, by Hedblom and many others in every respect that he indicated.

There is one point in which I do not quite agree with his conclusions, and that is merely an academic issue, a question of terminology. I object to calling spirochetal disease the cause, the etiology, of chronic abscess of the lung and of bronchiectasis just because it happens to be found in a high percentage of cases. I am sure that Dr Smith would not say, for instance, just because he found 60, 70, 80 or 90 per cent of all tonsils chronically diseased infected with spirochetes that spirochetes were the cause of tonsillitis. I think the stand to take is that the spirochetal disease is a secondary contaminant and that it is responsible for the disease, that is, for the chronic stages of the disease.

Dr Hedblom has pointed out that in most cases there is probably a lesion in the bronchial tree to start with, a *locus minoris resistentiae*, so to speak, on which the organisms can implant themselves and proceed to destroy the bronchial tree still further to cause the exacerbations. We pointed out that they appear in the exacerbations.

He has chosen a rather unfortunate animal for his experimental work because the rabbit is very susceptible to spirochetal disease. In the rabbit the introduction of spirochetes is quickly followed by necrosis and destruction of the tissues. The dog represents a different picture. In the dog it is difficult to produce a bronchiectasis or an abscess, a chronic lesion, of the virgin lung by means of spirochetes. We have been able to produce chronic lesions with the spirochetes in the dog but only after we have produced a *locus minoris resistentiae*, an acute abscess, or some other lesion by burning the bronchus beforehand and then implanting the organisms on that lesion. I think that that is the main issue. The bacteria form a very important part of the disease but they represent a secondary contamination and are the means by which the diseases are mainly propagated.

DR DAVID T SMITH, Rav Brook, N. Y. The point Dr Lord brought up is a pertinent one and I think I can illustrate what I wish to say much better than I can describe it. I have been engaged for four years in an attempt to isolate all the organisms involved in abscess of the lung and bronchiectasis and to recombine them so as to determine the combination necessary to reproduce the disease.

The slide shown is an illustration of a culture of *T. macrodentum*. I have also isolated a few strains of the larger *T. macrodentum*. These organisms in pure culture are absolutely harmless to animals.

The next slide is that of a pure culture of the large fusiform bacillus. I have isolated a number of strains of this and several small forms of fusiform bacilli.

I have isolated several cultures of the vibrio. In one culture I must have had something wrong with the salt content of the medium, for all the flagella became hypertrophied to such an extent that they could be seen readily with the dark-field apparatus.

I found a number of different kinds of cocci in these cases of abscess and bronchiectasis. The cocci produce simple pyogenic lesions when introduced into animals.

The various combinations of these organisms were tested. Neither spirochetes nor fusiform bacilli alone produced disease. The combination of the two likewise failed to produce disease. With the anaerobic hemolytic streptococcus, a little pus developed in the groin of a guinea-pig, but no necrosis and no foul odor. When the vibrio was added to the streptococcus, a much more extensive lesion was obtained, but still no necrosis and no odor. The addition of the fusiform bacillus to the coccus and the vibrio resulted in a small amount of necrosis, but no odor. The addition of the spirochetes to the coccus, vibrio and fusiform bacillus gave a severe lesion with extensive necrosis and foul odor. The resulting disease could then be transferred from pig to pig almost indefinitely.

That, of course, brings up the question which is in everybody's mind as to whether these spirochetes are secondary invaders. The spirochete is not secondary to the others. It is a concomitant rather than a secondary infection, that is, the spirochetes and fusiforms, vibrios and cocci all go down together into the lungs. Aspiration of the cocci alone results in a simple pyogenic infection of the lungs.

As Dr. Hedblom has pointed out, bronchiectasis does at times follow (1) acute infections of childhood, (2) pneumonia and (3) aspiration of foreign bodies. But bronchiectasis is not a constant sequela in these conditions, so it is more logical to suppose that only those patients develop bronchiectasis who are so unfortunate as to aspirate some of the anaerobic organisms from the mouth during the course of the disease. Congenital bronchiectasis, of course, is a possibility, but I fear that I cannot agree with Sauerbruch that it is a common observation since it is encountered rarely in routine necropsies on infants. I am afraid Sauerbruch has not distinguished clearly between congenital bronchiectasis and bronchiectasis beginning in early childhood as an infectious process.

I heartily agree with the two points mentioned by Dr. Hedblom in regard to treatment. If this work means anything at all it means that the organisms present in pyorrhea have something to do with bronchiectasis, abscess of the lung and gangrene. The best method of preventing them is to prevent these organisms getting into the lung. Personally, I feel that arsenic therapy is of some value in all cases of bronchiectasis and of great value in certain cases. In the last five years, we have found a number of cases, some of which are still under observation, in which excellent results were obtained by postural drainage and arsenic therapy. The patients were given postural drainage for from three to six months before treating them with arsenic, so that those who were going to get well by posture drainage alone could be eliminated. Then arsenic therapy was added and a number made a spectacular recovery.

I am glad Dr. Van Allen brought up the question of the relative susceptibility of the rabbit and the dog to these organisms. It is true that the rabbit is more

susceptible than the dog, but man also is very susceptible, and in this respect may be more like the rabbit than the dog. On the other hand, the dog is not completely resistant since abscesses have been produced in dogs with these organisms by Dr. Van Allen himself, by Duft Allen, Crowe and Scharff, Johannides and Hedblom, Harkey, and Widelein and Schleuter.

Atelectasis is a factor in the development of certain cases of abscess and bronchiectasis, as Dr. Coryllos has pointed out. These are anaerobic organisms and do not readily survive on the surface of the bronchus, that is, they cannot live on the surface of a bronchus as a streptococcus or an influenza bacillus can. They either disappear completely and leave no disease or they invade deeply into the bronchial wall, where they destroy the elastic tissue and produce a bronchiectasis.

# CHANGES IN THE PULMONARY CIRCULATION INDUCED BY EXPERIMENTALLY PRODUCED ARTERIO- VENOUS FISTULA

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AND  
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The altered hemodynamics of the pulmonary circulation in response to an increase in the volume flow of blood have been subjected to experimental observation through several different methods. The most direct studies have been made with a Starling heart-lung preparation<sup>1</sup> or a modification thereof. In these preparations the lung is a surviving organ isolated from any possible control by the central nervous system, and deductions as to the state of affairs in the intact organism are to be drawn with caution. Ligation of one branch of the pulmonary artery has been employed as a device to increase the volume flow in the contralateral lung,<sup>2</sup> but this method also has its obvious limitations. Wiggers<sup>4</sup> augmented the venous return to the heart by the intravenous injection of saline solution, again a method that is at variance with normal physiologic occurrences.

In the experiments herewith reported the venous return to the heart and consequently the volume flow of blood through the lungs have been increased experimentally by the opening of an arteriovenous fistula inserted in the systemic circuit. This procedure has been carried out on normally breathing cats and closely simulates as far as volume flow is concerned, what happens when a previously resting person undertakes moderate exercise. In contrast to what occurs in exercise, it may be pointed out that the establishment of an arteriovenous fistula entails a slight fall rather than a rise of pressure in the systemic circuit,

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1 Fuhner, H. and Starling, E. H. Experiments on the Pulmonary Circulation, *J. Physiol.* **47** 286 1913-1914

2 Drinker, C. K., Churchill, E. D. and Ferry, R. M. The Volume of Blood in the Heart and Lungs. *Am. J. Physiol.* **77** 590, 1926

3 Churchill, E. D. The Effect of Increased Blood Flow on the Ratio Between Oxygen Consumption and Pulmonary Ventilation. *Am. J. Physiol.* **86** 274, 1928. Haggart, G. E., and Walker, A. M. The Physiology of Pulmonary Embolism as Disclosed by Quantitative Occlusion of the Pulmonary Artery. *Arch. Surg.* **6** 764 (May) 1923. Scarff, J. E. Pulmonary Blood Pressures. An Experimental Study, *Arch. Surg.* **12** 591 (Feb.) 1926

4 Wiggers, C. J. Observations on the "Effective" Pressure in the Right and Left Auricles, *Am. J. Physiol.* **33** 13, 1914

and, secondly, that the blood returning to the lungs is richer rather than poorer in oxygen and presumably has a reduced rather than an increased content of lactic acid. The fall in aortic pressure results from the diminution in peripheral resistance occasioned by opening the fistula. This lowering of the aortic pressure undoubtedly diminishes the fraction of the total cardiac output that returns to the right side of the heart after traversing the coronary circulation.<sup>5</sup> In the experiments to be described the volume of blood actually flowing through the lungs has been determined by the Fick method,<sup>6</sup> and any change in the coronary fraction brought about by the fall in systemic pressure need not be considered in the calculations. That moderate variations in aortic pressure produce no "back pressure" effects through the pulmonary circuit on the pulmonary artery pressure has been shown by Anrep and Bulatao<sup>5</sup> in heart-lung preparations and confirmed by Katz and Wiggers<sup>7</sup> in the intact animal.

The arteriovenous fistula has been used in these experiments solely as a method of increasing the venous return to the heart. The numerous physiologic effects of such a fistula have been admirably studied by several workers,<sup>8</sup> but no experiments are recorded that deal with the effect of such an anastomosis on the pulmonary circulation.

#### METHOD

Drinker heart preparations<sup>9</sup> were made in cats anesthetized with sodium barbital. Cats so prepared breathe naturally with the heart exposed in an open pericardium sutured to the wall of the chest. A diagram of the complete preparation is shown in figure 1. The tracheal cannula was connected with a closed oxygen metabolism system containing sensitive valves (*H*), a spirometer (*G*) and a soda-lime chamber (*I*). The excursions of the spirometer were recorded on the kymograph (*C*) and gave a direct indication of the consumption of oxygen. Blood samples were taken by right and left ventricular punctures, which may be carried out under direct vision as the heart is fully exposed.

5 Anrep, G. V., and Bulatao, E. Observations on the Pulmonary Circulation, *J. Physiol.* **60** 175, 1925.

6 Fick, quoted by Dock, W., and Harrison, T. R. The Blood-Flow Through the Lungs in Experimental Pneumothorax, *Am. Rev. Tuberc.* **10** 534, 1925.

7 Katz, L. N. and Wiggers, C. J. The Influence of High Systemic Blood Pressures on the Right Ventricle and Pulmonary Circuit, *Am. J. Physiol.* **82** 91, 1927.

8 Holman, Emile. Experimental Studies in Arteriovenous Fistulas. I. Blood Volume Variations, *Arch. Surg.* **9** 822 (Nov.) 1924. Holman, Emile and Kolls, A. C. II. Pulse and Blood Pressure Variations. *Arch. Surg.* **9** 837 (Nov.) 1924. Holman, Emile. III. Cardiac Dilatation and Blood Vessel Changes. *Arch. Surg.* **9** 856 (Nov.) 1924. Lewis, T. and Drury, A. N. Observations Relating to Arterio-Venous Aneurisms. I and II, *Heart* **10** 301, 1923.

9 Drinker, C. K. A Useful Heart Method. *J. Exper. Med.* **33** 675, 1921.

The pressure in the carotid artery (*A*) was recorded by a mercury manometer (*B*). The pressure in the pulmonary artery was obtained by using a special cannula (*E*) inserted directly into the main stem of the artery just beyond the valves<sup>10</sup>. It was connected through a saline system with a manometer (*F*) having an extremely light cork float so that pressure excursions were written directly on the kymograph in centimeters of saline solution.

The arteriovenous fistula was established by the use of a specially blown double glass cannula (*D*), the apertures of which were tied into the femoral artery and vein in the groin. Opening and closing of the fistula were readily accomplished by removing and reapplying delicate artery clips. A saline wash bottle attached to the cannula enabled it to be filled before the start of the experiment and flushed out frequently in order to avoid the clotting that occurred at times despite the fact that heparin had been given intravenously.

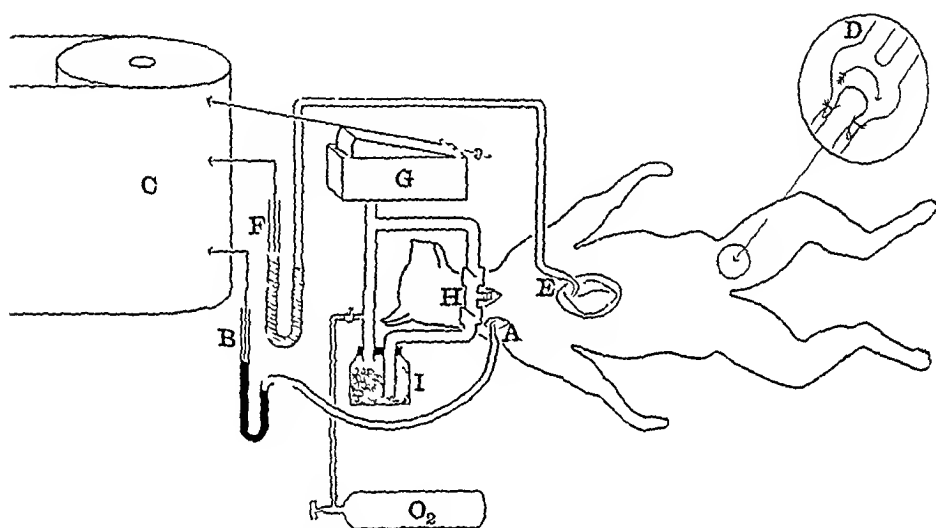


Fig 1—Diagram of apparatus, showing *A*, cannula in the carotid artery, *B*, mercury manometer, *C*, kymograph, *D*, double glass cannula in femoral artery and vein, *E*, cannula in pulmonary artery, *F*, saline manometer, *G*, Krogh spirometer, *H*, inspiratory and expiratory valves, *I*, soda-lime chamber

#### PROTOCOL

The following is a protocol of an experiment in which determinations of the blood flow were made

*Experiment 14* (March 21, 1930) —Weight of cat, 3.69 Kg

- 10 20 a m Anesthesia induced with chloroform and ether
- 10 31 a m 8 cc of 10 per cent sodium barbital injected into right external jugular vein Ether discontinued
- 10 37 a m Cannula inserted into left carotid artery
- 10 39 a m Blood pressure, 144 mm of mercury
- 10 43 a m 2 cc of sodium barbital injected intravenously

10 Swift, W. E., Haggart, G. E., and Drinker, C. K. A New Method for Measuring the Pressure in the Pulmonary Artery, *J. Exper. Med.* **36**: 329, 1922

- 10 47 a m Artificial respiration started for Drinker heart preparation  
 11 17 a m Artificial respiration discontinued Heart preparation complete  
 Animal breathing naturally  
 11 24 a m Double cannula (arteriovenous fistula) tied in left femoral artery  
 and vein  
 11 25 a m Tracheal cannula connected with metabolism system  
 11 27 a m Rate of oxygen consumption determined  
 11 34 a m Blood sample taken from right ventricle  
 11 35 a m Blood sample taken from left ventricle  
 11 50 a m Cannula inserted into pulmonary artery  
 11 55 a m Approximately 100 mg of heparin in 10 cc of saline solution  
 injected into femoral vein  
 12 09 p m Carotid artery pressure, 116 mm of mercury Pressure in pul-  
 monary artery, 188 cm of saline solution  
 12 10 p m Arteriovenous fistula opened Carotid artery pressure, 98 mm of  
 mercury Pressure in pulmonary artery, 205 cm of saline solution  
 12 11 p m Arteriovenous fistula closed and washed out  
 12 19 p m Arteriovenous fistula opened Consumption of oxygen determined  
 12 20 p m Arteriovenous fistula closed and washed out  
 12 27 p m Arteriovenous fistula opened  
 12 28 p m Blood sample taken from right ventricle  
 12 31 p m Blood sample taken from left ventricle

Experiment ended Rectal temperature constant at 39 C throughout the  
 experiment

### RESULTS

The results obtained in experiment 14 were as follows

Before opening arteriovenous fistula

Oxygen consumption	= 30.8 cc per minute
Oxygen capacity of arterial blood	= 16.56 per cent by volume
Oxygen content of arterial blood	= 15.01 per cent by volume
Oxygen content of venous blood	= 6.62 per cent by volume
Difference in oxygen content	= 8.39 per cent by volume
Calculated rate of blood flow (Fick)	= 367 cc per minute

With open arteriovenous fistula

Oxygen consumption	= 32.7 cc per minute
Oxygen capacity of arterial blood	= 13.81 per cent by volume
Oxygen content of arterial blood	= 13.58 per cent by volume
Oxygen content of venous blood	= 7.96 per cent by volume
Difference in oxygen content	= 5.62 per cent by volume
Calculated rate of blood flow (Fick)	= 584 cc per minute
Increase in blood flow	= 217 cc per minute or 59 per cent

The pressure in the pulmonary artery was determined fifty-three  
 times in seventeen experiments both before and after the arteriovenous  
 fistula was opened There was invariably a slight rise in pressure on  
 opening the fistula and a fall to the previous level on closing The  
 average rise in pressure was 1.7 cm of saline solution The smallest  
 increase was 0.6 cm and the greatest increase 3 cm



Figure 2 is a kymographic tracing showing the effect of opening the arteriovenous fistula on the systemic and pulmonary artery pressures and on the pressure in the left auricle. A cannula inserted into the left auricle was connected with a wide bore saline manometer at the top of which was a small Biot's bellows recorder. The upper tracing

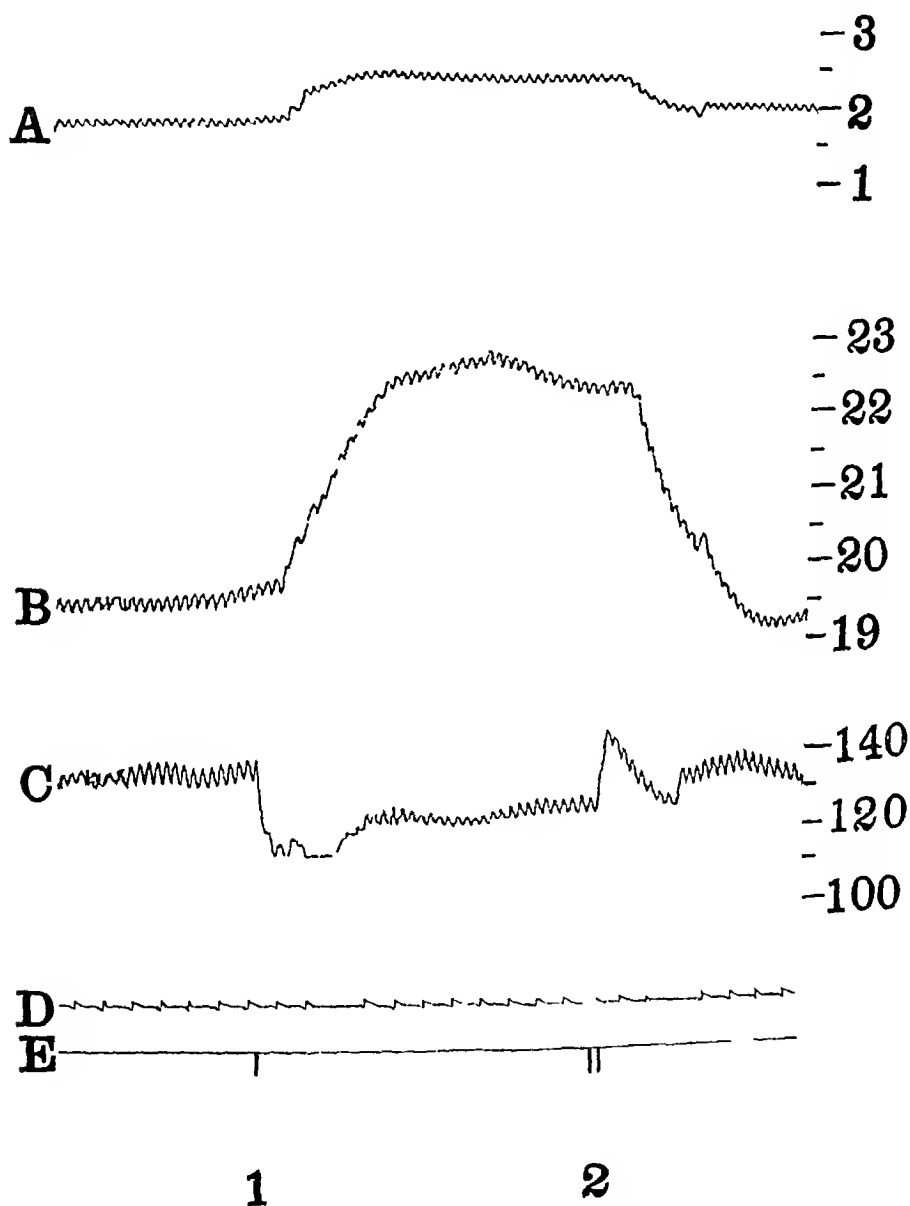


Fig 2—Kymographic tracing from experiment 21, showing *A*, tracing of left auricular pressure calibrated in centimeters of saline solution, *B*, pulmonary artery pressure in centimeters of saline, *C*, carotid artery pressure in millimeters of mercury, *D*, time in 5 second intervals, *E*, signal magnet. At 1 the fistula between the femoral artery and vein was opened. At 2 the fistula was closed.

(*A*) shows the pressure changes in the left auricle calibrated in terms of centimeters of saline solution. The middle tracing (*B*) is that of the pressure in the pulmonary artery, also in centimeters of saline solution.

tion The lower tracing (C) is that of the systemic blood pressure recorded in millimeters of mercury At 1 the fistula between the femoral artery and vein was opened, and at 2 closed When the fistula was opened, there was a fall of 10 mm of mercury in the systemic blood pressure, a rise of 3 cm of saline solution in the pressure in the pulmonary artery and a rise in left auricular pressure of 0.7 cm of saline solution

In five experiments complete determinations of the blood flow were made The results are tabulated in the accompanying table It is evident that the circulation rates are below the normal resting levels for cats of similar weight that have not been subjected to operation This may be attributed to the loss of blood attendant on the operation and the exposure of the heart to atmospheric pressure The increase in the volume flow of blood through the lungs on opening the arteriovenous

*Results of Complete Determinations of the Blood Flow*

Cat	Weight, kg	Circulation Rate Before Opening Arterio- venous Fistula, Cc per Minute	Circulation Rate with Open Arterio- venous Fistula, Cc per Minute	Increase, Cc per Minute	Per Cent of Increase	Pulmonary Artery Pressure Before Opening Arterio- venous Fistula Cm of Saline	Pulmonary Artery Pressure with Open Arterio- venous Fistula, Cm of Saline	Increase Cm of Saline	Per Cent of Increase
5	3.55	268	331	63	24	13.0	14.0	1.0	8
9	2.15	260	376	116	45	19.8	20.8	1.0	5
11	4.13	429	610	181	42	20.5	22.5	2.0	10
14	3.69	367	584	217	59	18.8	20.5	1.7	9
15	3.31	289	409	120	42	14.5	16.3	1.8	12

fistula varies between 24 and 59 per cent in the different cats The rise in pressure in the pulmonary artery is of slight magnitude in comparison, varying between 5 and 12 per cent If the resistance in the pulmonary circuit were constant an increased blood flow through the lungs would cause a proportionate increase in pressure in the pulmonary artery That the rise in pressure in the pulmonary artery in these experiments was slight and by no means proportional to the increase in volume flow of blood indicates a decreased resistance in the pulmonary circuit How such a decrease in resistance is brought about has not been demonstrated It may be attributed to the passive dilatation of the vascular bed of the lungs or to opening of new pathways in response to the increased head of pressure It is also possible that some mechanism exists that brings about an active change in the tonus and caliber of the pulmonary vessels

The conditions inherent in the experimental method employed give assurance that the decreased resistance of the pulmonary circuit in these experiments cannot be due to the chemical changes in mixed venous

blood which occur during muscular activity. The arteriovenous communication simulates exercise by increasing the volume flow of blood through the lungs, but paradoxically changes the chemical composition of mixed venous blood in a direction opposite to the changes brought about by muscular activity. The results of these experiments suggest, therefore, that the pulmonary circuit adapts itself to an increased volume flow of blood by a rise in pressure in the pulmonary artery and a lowering of resistance in the pulmonary vascular bed. It seems probable that the latter is a passive phenomenon.

#### SUMMARY

An arteriovenous fistula in the systemic circuit has been used as an experimental method for increasing the volume flow of blood through the lungs of normally breathing cats. Determinations of the blood flow and measurements of pressure in the pulmonary artery have been made.

In five experiments, the volume flow of blood through the lungs increased from 24 to 59 per cent on opening the arteriovenous fistula.

The pressure in the pulmonary artery invariably showed a slight rise on opening the fistula.

The slight increase in pressure in the pulmonary artery associated with a considerable increase in circulation rate suggests a compensatory lowering of resistance in the pulmonary circuit.

#### ABSTRACT OF DISCUSSION

DR JOHN H. GIBBON, JR., Boston. I am glad that Dr. Corvillo spoke of Dr. Wearn's work on the capillaries of the lung. We have not, of course, in this experimental study, determined how the decrease in pulmonary resistance occurs, i. e. whether it occurs by the opening up of new capillaries or by relaxation of the pulmonary arterioles.

# OBSTRUCTIVE PULMONARY ATELECTASIS

PROBLEMS OF PATHOGENESIS AND CLINICAL MANAGEMENT \*

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When bronchial obstruction develops, as by accumulation of mucus from inflamed membranes, and evacuation fails, the air imprisoned in the lung is absorbed and atelectasis results. This has been demonstrated by repeated and well controlled observations in man and in experimental animals. Methods of prevention and treatment aim to free the lower airways from material by stimulating the natural expelling forces or by instrumentation and to aerate the lung with deep breathing. Thus the theory of the pathogenesis and clinical management of obstructive pulmonary atelectasis is clear on the face of it.

When the phenomena are examined in detail, however, they appear complicated and confused. Opposite effects may result from circumstances that are seemingly identical, and this may occur in the same individual simultaneously in separate parts of the lungs. Contradictory results are seen especially in the action of cough on bodies obstructing the bronchi and in collapse of the lung after obstruction. Thus, cough may or may not raise the secretions, and may even drive them farther into the lung, complete bronchial blockage leads quickly to atelectasis on one occasion, and produces no reduction of the pulmonary air content on another.

Our purpose in this paper is to review the experimental and clinical data of obstructive atelectasis so far as necessary to set forth gaps and inconsistencies, and then to indicate a solution to some of these problems by reference to a principle of respiratory function that we have demonstrated recently <sup>1</sup>.

It will be necessary, first, to define and explain certain terms to be used.

Atelectasis refers to an airless state of the lung with collapse of the alveoli. No reference is implied to consolidation by replacement of air with exudate, transudate or other substance <sup>2</sup>. Obstructive atelectasis,

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\* From the Department of Surgery, Yale University School of Medicine.

1 Van Allen C, Lindskog G and Richter H. Yale J Biol & Med 2: 297, 1930. work ready for publication.

2 The more inclusive term apneumatosiis used by Corvillo (Postoperative Apneumatosiis [Atelectasiis] and Postoperative Pneumonia, I A M A 93: 98 [July 13] 1929) carries these implications.

already defined, is distinguished from the compressive type, in which the alveoli are collapsed by pressure from without, and the fetal type, in which there is persistence of the prenatal airless condition. Reference to bronchial obstruction will apply only to that from fluids, for the sake of definite example. The obstruction is referred to as partial when the cross-section of the bronchial lumen is incompletely filled, and air may pass in either direction, as total when the cross-section is completely filled and air cannot pass and as valvular when the arrangement is such as to permit air to pass in one direction only. In the last instance, the valve is spoken of as expiratory when exit is allowed and as inspiratory when entrance is allowed. The position of the obstructing plug in the bronchial tree is indicated as lobar when one or more entire lobes of the lung are shut off thereby, and as lobular when one part of a lobe is occluded. The term distal is used in relation to the bronchial tree to indicate the direction or part toward the alveoli from a given point, while proximal applies to the direction or part toward the trachea. The word air is used loosely to refer to the respired gases in general. The available air is an expression introduced to replace vital capacity, meaning that part of the air in the lung after the deepest inspiration which can be thrown out with one maximal expiration.

#### THE DEVELOPMENT OF BRONCHIAL OBSTRUCTION

The bronchial tree is provided with various means to maintain its patency, viz., cartilaginous stiffening in the walls of the larger passages, the dilating influence of the pulmonary muscular and elastic tissue, bronchial peristaltic and ciliary action, the ebb and flow of air in quiet or forceful respiration and gravitation.

The bronchi are known to undergo change of caliber synchronously with the phases of respiration, dilating during inspiration and contracting in expiration. The change is increased in forced breathing, and complete obliteration of the lumen may occur with cough<sup>3</sup> or in anaphylaxis<sup>4</sup>. Rhythmical constricting waves have been seen to pass along the bronchi in a proximal direction<sup>5</sup>. To what extent movements of the bronchial wall act to expel material lying in the lumen cannot be told from the evidence obtained, because the result is confused with that of ciliary expulsion. Radiopaque bodies have been seen to pass from the bronchi to the trachea in as short a time as twelve minutes<sup>6</sup>. Theoretically, the bronchial inspiratory enlargement may serve to dis-

3 Weingaertner, M. *Arch f Laryng u Rhin* **32** 1, 1920

4 Schultz, W., and Jordan, H. *J Pharmacol & Exper Therap* **2** 375 1911

5 Bullock, G., and Gottlieb, G. *Laryngoscope* **32** 284, 1922. Reinberg S

*Am J Roentgenol* **14** 354, 1925

6 Bullock and Gottlieb (footnote 5, first reference)

engage the wall from the obstructing body and loosen the attachment, while the expiratory constriction compresses and molds the body to a smaller diameter and squeezes it along the tube.

The eliminative action of the cilia is an entity definitely to be reckoned with, for there is direct evidence of its effects. In patients under general anesthesia, blood stains have been seen by bronchoscopy to travel from the cauda to the larynx in a few minutes.<sup>7</sup>

Passage of the respired air in quiet or forced breathing tends to loosen obstructions in its path and to move them along. Emphasis should be placed on the fact that the available air is responsible for

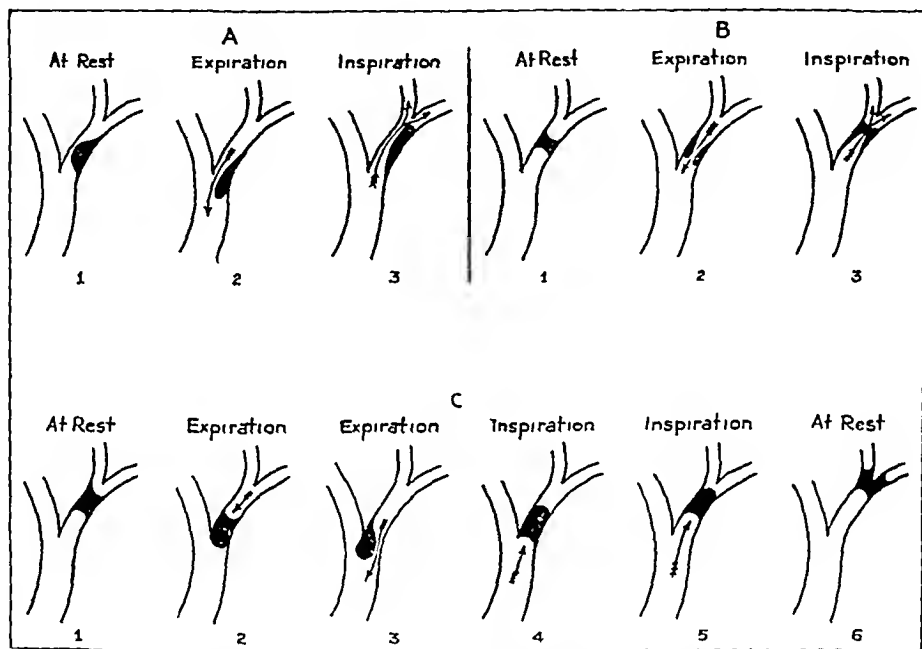


Fig. 1—Three varieties of the behavior of mucus obstructing the bronchial lumen under the influence of respired air. *A*, partial obstruction; *B*, 'doughnut' type of obstruction; *C*, expiratory valve type of obstruction.

the effects, and that the residual air is powerless to operate in an eliminative capacity. Thus an individual is able to execute the muscular effort and laryngeal movements of cough after a complete expiration, but no exclusion is accomplished. The available air is the ram that drives through the bronchi and trachea in coughing; all or a part of this may be used by one cough depending on excursion and force. Expulsion of substances from the bronchi depends on the expelling force superseding forces of adhesion. The behavior of sticky viscid fluid in various quantities in the bronchial tree in forced respiration is suggested by reference to figure 1. The drawings at *A* show partial

occlusion by a small mass lying in the bronchial lumen. With expiration, it is urged in a proximal direction, and it will be thrown toward the trachea if the force is sufficient. With inspiration, it is urged distally and may be transported into smaller passages, where total obstruction may result. At *B*, a larger mass fills the bronchial lumen at one point when at rest, but the amount is small enough and adhesion strong enough that at expiration thinning and rupture occur at the center, and the result is a partial occlusion.<sup>8</sup> At *C*, a still larger accumulation is present. Expiration pushes it along the bronchus to a point of sudden and considerable enlargement of the lumen at the entrance of a side branch. Sufficient force being active, it will be carried past this to become a partial obstruction in the larger passages beyond, but if adhesion is the greater force the mass may ride at the bifurcation while the air passes and drop back again at inspiration, refill the lumen and be carried into the periphery. This event, however, has brought about partial or complete loss of the available air from that part of the lung and the plug now assumes a position higher than before, or, if it resists distal displacement, suction is developed on its distal side in each inspiratory phase. Expiration is less able than before to effect expulsion in proportion to the amount of available air lost. The event may have had yet another result, for the cross-sectional area of the bronchial tree increases rapidly toward the periphery, and a plug that fills the lumen of a given bronchus may be unable to fill more than a part of its branches. The phenomenon of transportation of obstructions toward the periphery has been observed in man and in animals by the aid of fluoroscopy and the injection of iodized poppy seed oil 40 per cent.<sup>9</sup> It may be explained in part by the expiratory valve mechanism that has been described and in part by absorption of air distal to the obstruction and changes in pressure relationships from that source. Thus figure 2 gives curves of pressures that were obtained from the bronchial lumen at points just proximal and distal to a total plug occluding one lobe. Only the expiratory pressures are shown, and the purpose of the experiment was to determine the influences exerted by quiet and forceful breathing on a total plug. There was quiet respiration to begin with, and section *A* represents the two pressures when obstruction was instituted during expiration and loss of a part (tidal) of the available air. The levels are seen to be practically identical. At *B*, obstruction was relieved temporarily and then instituted at the height of inspiration. The inspired air was thus imprisoned behind the plug. The distal pressure

<sup>8</sup> This is the "doughnut" behavior described by Lee (personal communication) from bronchoscopic observations in man.

<sup>9</sup> Archibald, E., and Brown, A. *Am Rev Tuberc* 16:111, 1927.

level is seen to be above that of the proximal pressure. The situation was allowed to remain for observation, and it was found that the distal pressure gradually fell and in thirty minutes had reached the level of the proximal pressure. Presumably, the tidal air was being absorbed or otherwise lost. After this, the effect of cough was imitated by shutting off the trachea momentarily in the early stages of expiration and obtaining straining. Both pressures are seen to rise sharply, the proximal pressure to somewhat the higher point. The domination of

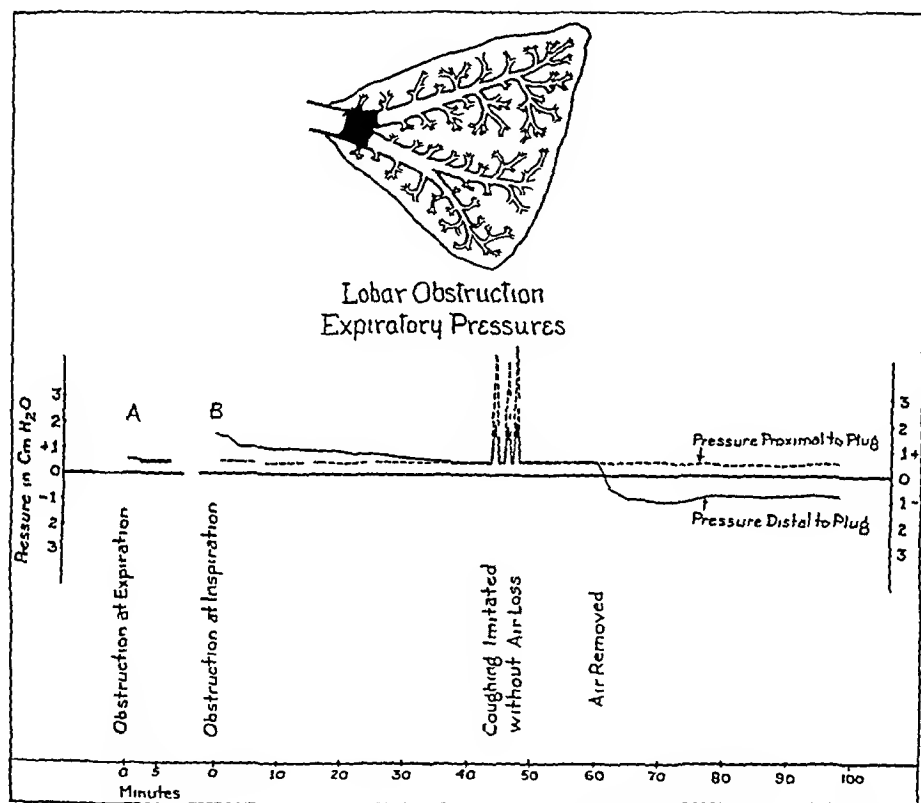


Fig 2—Plug producing complete lobar bronchial obstruction. Curves of expiratory pressures measured at points proximal and distal to the plug. Obstruction instituted at the end of expiration (A) and at the end of inspiration (B).

the proximal value was found to be a constant effect of straining to expire against resistance and to be proportional to the exertion of straining. After this maneuver the pressures returned to their former levels at equality with each other when they were noted to remain without noticeable change for a few minutes, about 5 cc of air was withdrawn by aspiration with a syringe from the occluded portion of the bronchial tree. The distal pressure is seen to drop at once below the proximal pressure and to maintain the lower level. These measurements show that in expiration the relation of the pressures distal and proximal to a bronchial obstruction filling the lumen totally at one



point depends on the amount of air imprisoned distal to the plug, and that the distal pressure predominates only when air previously inspired still remains. It has been found<sup>10</sup> that the distal pressure drops progressively as the imprisoned air is absorbed and atelectasis develops. The degree of suction then exerted on the plug toward the periphery of the lung is considerable. Under conditions of lowered distal pressure, coughing serves to increase the predominance of the proximal pressure.<sup>11</sup> Coughing can therefore be expected to expel a total plug only when a supply of air available for its action exists in the occluded portion of the lung, and this supply tends to be absorbed. With loss of the available air, cough is calculated to exert a driving effect toward the periphery.

This evidence of the dependency of cough and other expiratory functions on the available air of the obstructed portion of the lung for expelling effects appears to be directly contradicted by certain clinical experiences. Reliable observers<sup>12</sup> have reported that some patients with well developed massive atelectasis have been relieved of the condition after violent coughing and deep breathing. Thick tenacious mucus was coughed up at the time, and roentgen examination showed re-aeration of the lung. This contradiction will be discussed further after other problems have been presented.

#### THE DEVELOPMENT OF ATELECTASIS

Credit belongs to Lee and his associates<sup>13</sup> for the first satisfactory proof of the obstruction theory of atelectasis.<sup>14</sup> They occluded a part of the bronchial tree of a dog with thick mucus which had been aspirated from the bronchus of a patient with atelectasis, and they found that the corresponding portion of the parenchyma of the lung was atelectatic after three hours. Concentrated mucilage of gum acacia was used for the same purpose in four other dogs, and atelectasis was evidenced within from thirty minutes to three hours.<sup>15</sup> Coryllos, Hen-

10 Van Allen, C, and Adams, W. *Surg Gynec Obst* **50** 385, 1930

11 Lindskog, G, and Van Allen, C. Work ready for publication

12 Scott, W J M. Massive Atelectasis and Postoperative Pneumonia. Prophylaxis and Treatment, *J A M A* **93** 101 (July 13) 1929

13 Lee, W, Ravdin, I, Tucker, G, and Pendergrass, E. *Ann Surg* **88** 15 1928

14 Lichtheim (*Arch f exper Path u Pharmacol* **10** 54, 1878) is commonly credited with the first experimental reproduction of obstructive atelectasis. He confused atelectasis with pneumonia, however, and permitted pneumothorax to lapse of the lungs to enter into the circumstances of experiment to such an extent as to render the results unconvincing.

15 Complete proof, by postmortem examination, of the presence of atelectasis in their animals was obtained (personal communication to the authors), although a report was not published.

derson and their co-workers<sup>16</sup> obstructed the primary bronchus on one side in about sixty dogs with inflated rubber balloons and examined the lungs after a period of time which varied from one to twenty-four hours. Atelectasis of the occluded part was always found. Still others have obtained this condition after closure of the bronchus to one or more of the pulmonary lobes by ligature.<sup>17</sup>

Convincing evidence in denial of this causal relation of bronchial obstruction to atelectasis came to one of us (C V A<sup>10</sup>) in earlier work. The first was seen in a dog that was being used in experiments for another purpose. Two months before, the wall of a bronchus within the lower lobe of the right lung had been cauterized through a bronchoscope and completely destroyed for a length of about 1 cm. The lobe now presented the picture seen in figure 3. The bronchus was interrupted at the burned point by a solid sequestrum of necrotic tissue, and beyond this the bronchial lumen was filled throughout with glassy mucus, as evidence of total obstruction. Nevertheless the parenchyma was air-containing (fig 4) and could not be distinguished in this regard from that of unoccluded portions of the lung. In two other instances of the same sort, in which examination was made one and one and one-half months respectively after destruction of a bronchus, the lung again remained normally air-containing.

Other methods for obstructing the bronchi were then tested. Gum acacia mucilage, of the concentration used by Lee and his co-workers, was injected into the bronchial tree of the lower lobe of the right lung, and the dogs were maintained under anesthesia in order to depress the respirations and to ensure retention of the material. Three animals were so treated and then examined after a period of from three to twelve hours. No atelectasis resulted, although the bronchi remained "drowned" with the fluid. The rubber balloon method was rejected because of difficulty with deflation and instead a certain sticky and malleable rubber preparation (Michelin mastic) served the purpose well. Piece after piece of this was carried through a bronchoscope and pressed into the bronchi of the lower lobe of the right lung and accessory lobes, until they were distended with a branching cast which presented no possibility of slipping and admitting air. This type of obstruction was applied to four dogs and permitted to remain for

16 Corvillo P N. Postoperative Apneumotosis (Atelectasis) and Postoperative Pneumonia. *J A M A* **93** 98 (Jul 13) 1929. Corvillo P N and Birnbaum G L. Obstructive Massive Atelectasis of the Lung. *Arch Surg* **16** 501 (Feb) 1928. Lobar Pneumonia Considered as Pneumococcic Lobar Atelectasis of the Lung. *ibid* **18** 190 (Jan) 1929. Henderson Y, Haggard H W, Corvillo P N, Birnbaum G L and Radloff F. Treatment of Pneumonia by Inhalation of Carbon Dioxide. *Arch Int Med* **45** 72 (Jan) 1930.

17 Andrus W DeW. Cardiorespiratory Physiology Following Collapse of One Lung by Bronchial Ligation. *Arch Surg* **10** 506 (Jan) 1925.

periods up to twenty-four hours before the animals were killed. No atelectasis resulted.

The total variety of bronchial plug had thus failed after trial in different forms in ten dogs, and a test of obstruction was next made by means of an apparatus that had the effect of an expiratory valve. A dog was anesthetized and tracheotomized and a cork pierced by a tube, was slipped down the trachea and forced into a bronchus of the

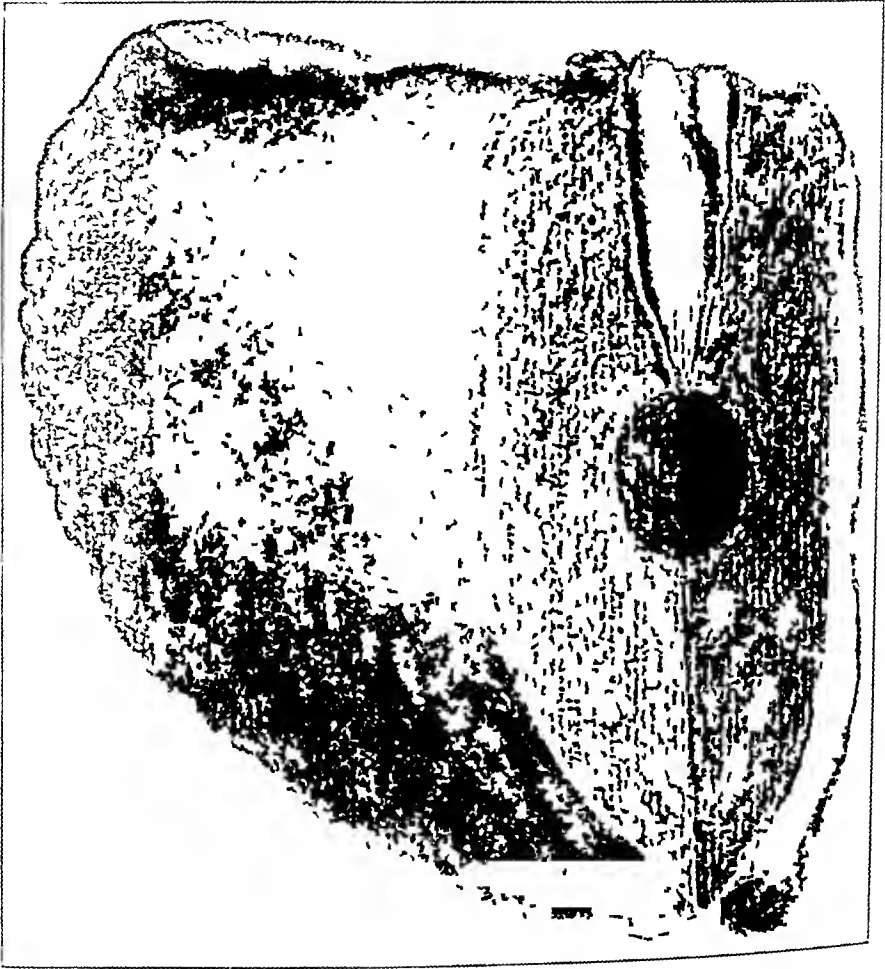


Fig. 3—Right lower lobe of a dog's lung. The bronchus has been opened, demonstrating complete lobular obstruction of the lumen caused by cauterization two months before the animal was killed. The bronchial tree distal to this point is filled with retained mucous secretion, and the parenchyma is air-containing.

lower lobe of the right lung. From this cannula a slender rubber tube was carried out of the trachea and connected to a glass nozzle. The tip of the nozzle was submerged just below the surface of water in a vessel. With first expiration an bubbled past the water valve in considerable quantity, with the second, a bubble or two passed, and after this (the available air having escaped) the bubbling ceased. The water meniscus in the nozzle fell with each expiration precisely to the level of the outlet, and rose about 10 cm. with inspiration. These level-

remained constant, as nearly as could be detected, for six hours. At autopsy, the cork was found so tightly engaged in the bronchus that the tissues had to be cut to free it, and yet the obstructed portion of the lobe was fully air-containing. Three other dogs treated in this way behaved similarly.

In an experiment of this type with a cork and water valve the tracheotomy opening became partly closed by a blood clot. This was not discovered until it had been in effect for some time and had given rise to labored respiration. After four hours, the animal was killed, autopsy revealed complete atelectasis of the obstructed lobe of the

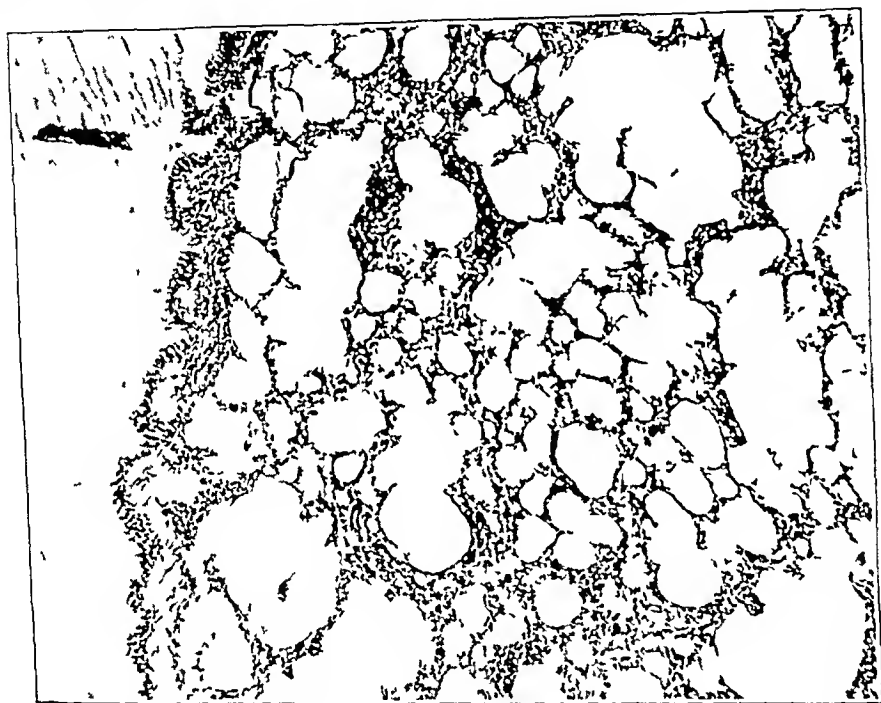


Fig 4—Microscopic appearance of the parenchyma of the lung specimen shown in figure 3, in the obstructed part. The alveoli are air-containing, and at one side is a bronchus filled with secretion.

lung. The factor of resistance in the trachea was then applied to other dogs, impediments of other sorts being substituted for the blood clot, such as gauze sponges or partial closure of the trachea by clamping. Atelectasis formation then became the rule. Analysis of the situation showed that the effect was obtained by resistance applied to the expired air passing through the trachea, and the type of respiration thus produced appeared similar essentially to that of coughing, moaning, grunting etc. in which the vocal cords approximate and resist expiration. We have referred to this as straining respiration. Its presence in these experiments was found essential to the development of atelectasis whether the plug was total or equipped with a valve, and the

reason for this remained undetermined. The valve, indeed, played no part other than to permit the available air to escape and to hasten by so much the advent of atelectasis.

After this, the apparatus<sup>18</sup> and method for occluding the bronchus were refined, to permit more precise selection of the point of occlusion and reduction of trauma. It became possible to apply obstruction to various parts of the bronchial tree and more precisely than hitherto, immediately confusion entered into the results, for straining respiration then failed in some instances to effect atelectasis. In some experiments atelectasis developed, and in others in which no difference existed that could be detected, except for the position of the plug, the lung remained perfectly air-containing. Analysis of a series of tests showed that atelectasis occurred when the plug involved one or more lobes (lobar obstruction) and failed when only a part of one lobe was included (lobular obstruction). This is illustrated by the roentgenogram reproduced in figure 5. Three of the pulmonary lobes are depicted after removal from a dog twenty-four hours following the application of two bronchial plugs (surgical bone wax introduced by bronchoscopy). The plug at *A* is lobar and that at *B* is lobular. Atelectasis appears only at *A*. A review of previous experiments now disclosed the fact that when record had been made of this point the instances of atelectasis were those with lobar obstruction. The cause for the difference in the results of lobar and of lobular obstruction was not at once apparent.

The situation presented by our data up to this time, regarding the factors of the type of respiration and the position of obstruction, is summarized in figures 6 and 7. The amount of atelectasis produced and the period of time of each bronchial plug used are represented by a single dot or circle. Figure 6 refers to experiments with free respiration throughout, and the dots indicate lobular, and the circles lobar, plugs. It is seen that atelectasis occurred in lobar obstruction only and not until, after twenty-four hours. Under these circumstances however, the occurrence was not constant. Figure 7 presents the experiments with straining respiration, and the same designation of lobular and lobar positions is used. Atelectasis is noted again in lobar obstruction only, but here it is seen to have appeared to some extent in nearly all cases and to have reached extensive developments often at early periods.

The results of these experiments demonstrate, further, that aside from the influence that the type of respiration and the position of the obstruction exert, the incidence and rate of atelectasis formation after total bronchial occlusion in a twenty-four period are variable to the extent of 100 per cent. No explanation for this has been found.

<sup>18</sup> Van Allen C. Yale J Biol & Med 2 295, 1930

## THE PRINCIPLE OF AIR EXCHANGE BETWEEN THE PARTS OF A LOBE

Certain deductions from these experiments have led to other experiments and the demonstration of a principle of respiratory function which pertains to the behavior of air in the lung beyond a bronchial obstruction and which serves to explain some of the contradictions at hand. Details of the proof and character of this are furnished elsewhere.<sup>1</sup> The principle may be stated briefly as follows:



Fig 5—Roentgen appearance of three lobes of a dog's lungs after bronchial obstruction by wax plugs for twenty-four hours. *A*, complete lobar obstruction, followed by atelectasis; *B*, complete lobular obstruction, with maintenance of aeration. A test with high pressure showed these plugs to be air-tight.

The partitions that divide one alveolus from another and one lobule from the next in a single lobe of a lung permit air, fluids and finely particulate matter to pass. This exchange is a result of very slight differences in pressure within two adjoining lobules (the difference may be as low as 1 cm of water pressure), these differences are such as are commonly generated between obstructed and free parts of the bronchial tree during quiet breathing. It has been found that an

obstructed portion of one lobe "breathes" by means of this communication through adjacent free parts, and that the amount of this respiratory interchange may be as much as 3,600 cc per hour. The interchange is found to occur in man, the dog, cat and rabbit by tests made in vitro. The methods for testing during life are applicable to the dog only, and in this animal the phenomenon is regularly obtained. It fails to occur between lobes.

The mechanism of this passage is not clear. Diffusion may account for it, but the fact that a particulate substance (India ink) is admitted indicates that there must be anatomic connections. These are evidently

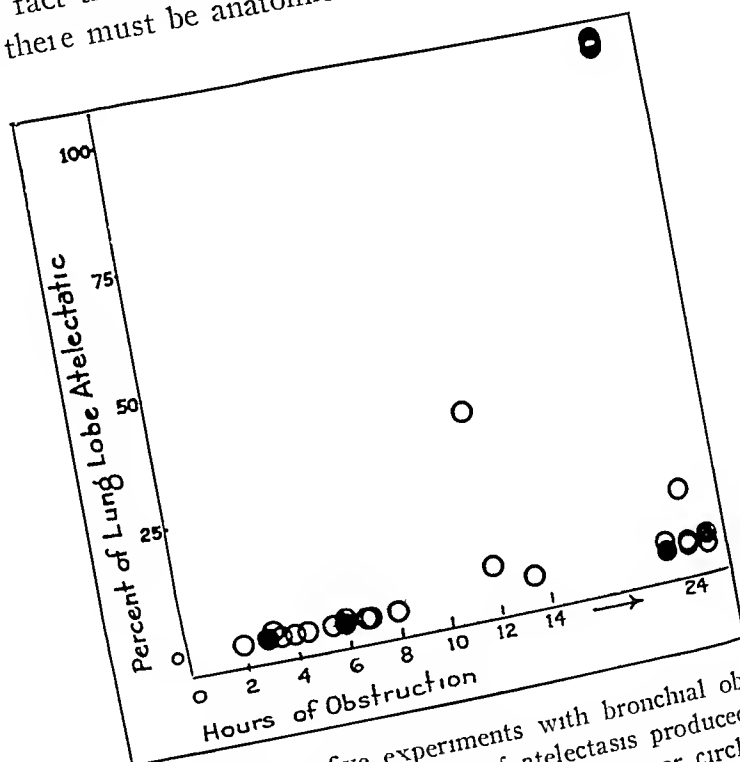


Fig 6—Results of twenty-five experiments with bronchial obstruction in the presence of quiet breathing. The amount of atelectasis produced and the period of obstruction in each case are indicated by a single dot or circle. Dots refer to complete lobular obstruction and circles to complete lobar obstruction.

in the periphery of the lung, and they may be the alveolar wall pores recently described by Ogawa<sup>19</sup> as to position, shape and construction.

#### INTERPRETATION

The free intercommunication that exists between the anatomic units of a lobe of a lung appears to play a determining part in the mechanism of both bronchial obstruction and atelectasis formation. To assist in understanding the function, an analogy may be drawn to the exchange of fluid by anastomosis in the blood and lymph vascular systems, which

<sup>19</sup> Ogawa, C. *Am J Anat* 27 333, 1920

permits one unit to compensate for interruption that may occur in the supply channel of the other. In the bronchial system of one lobe, blockage of a part leaves others to ventilate the parenchyma. This compensation fails when all bronchi of a lobe are occluded (lobar obstruction).

The inconsistencies appearing in the action of cough are removed by consideration of this circumstance. As has been emphasized, cough depends for eliminative effect on the presence of available air in the lung behind the bronchial obstruction. The inspiration that precedes the cough furnishes air to the obstructed lung past the plug, if that is

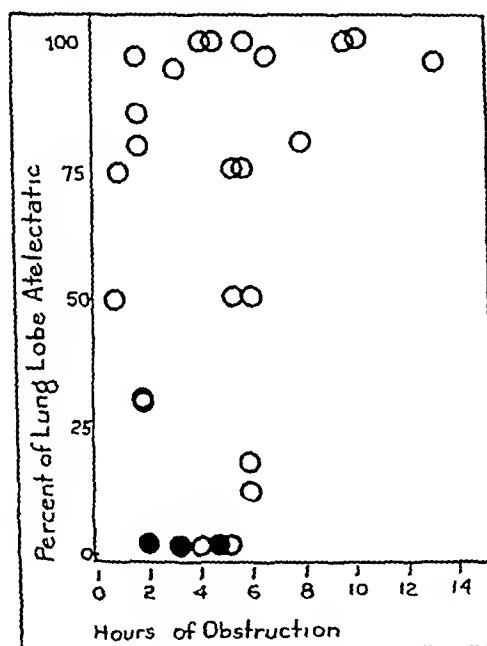


Fig 7—Results of twenty-seven experiments with bronchial obstruction in the presence of straining respiration. The same method of designation is used as in figure 6.

partial or of the inspiratory valvular type, or by way of the peripheral intercommunications, if the plug is total and lobular. Under these circumstances, the cough builds up a higher pressure in the bronchial lumen distal to the plug than in that proximal to it, and may move the obstruction toward the larynx. This is illustrated by the curves shown in figure 8, from pressures measured at points just distal and proximal to a total lobular bronchial plug. The expiratory pressures only are shown. The distal pressure lies above the proximal value, and this relationship persists during quiet respiration throughout. When the action of cough was imitated, both pressures rose abruptly and fell, producing an increase in the advantage of the distal value. Again, on the removal of about 10 cc of air from the bronchial tree beyond the



plug, no disturbance resulted in the relation between the two pressures. This behavior contrasts with that of the air in a lobar total plug, as has been described (fig 2), for then the inspiration that precedes the cough does not furnish air to the obstructed lung, and if the available air already in that part has been lost by absorption or other means, the cough is unable to raise the distal pressure above the value proximal. It should be remarked that this distinction between the lobular and the lobar positions of obstruction in the effectivity of cough refers as well to lobular plugs that are with and without functioning intercommuni-

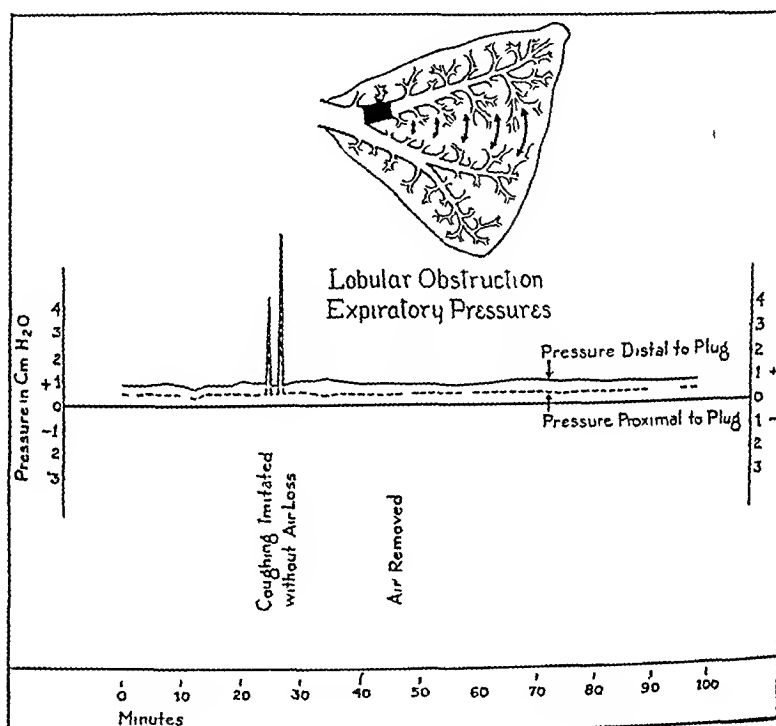


Fig 8—Plug producing complete lobular bronchial obstruction. Curves of expiratory pressures measured at points proximal and distal to the plug. Obstruction was instituted at the end of inspiration.

cation. Thus it has been found that one part of a lobe may become isolated by a multiplicity of mucous plugs, so that the behavior of the imprisoned air is the same as that in lobar obstruction.

The importance of the peripheral intercommunication for routine maintenance of the patency of the bronchi is evident when one contemplates the extreme fineness of the peripheral airways, the lack of mural rigidity and of ciliary apparatus and the tendency to secretion and exudation. A minute drop of fluid must serve to obstruct a respiratory duct. Were it true, as generally believed, that the duct ends in a blind cluster of alveoli, consider the situation that arises—

when the duct becomes occluded during sleep or at other times when expelling forces are not soon instituted. The available air would soon be absorbed, and the opportunity for expulsion of the block would be lost. The obstruction must remain. As it is, with exchange of air between the alveoli, expulsion is possible with each expiratory effort. As a matter of fact, during shallow respiration the communications may not function after bronchial blockage, and the part remains isolated until a deep breath or two is taken. After that, exchange of air is instituted and continues in effect. This has been a common observation, and may be explained by supposing that the alveoli in some parts are not used in shallow breathing and partly collapse with the result that they cannot serve for the purpose of intercommunication without first a full inspiration to expand them. The deep breath or yawn that follows on prolonged quiet occupation or on awaking from sleep may have the purpose of expanding functionless regions of the parenchyma for the aeration and unburdening of occluded parts.

The development of atelectasis following bronchial obstruction must depend primarily on the rate of two processes, i.e., loss of air and accession of air. When the rate of loss is in excess, atelectasis results. The questions of the position of the obstruction and the efficiency of the peripheral communications are therefore of prime importance. Atelectasis may develop only when the obstruction is lobal or when it is lobular and the communications to that portion of the lung are partly or wholly closed and unable to keep pace with loss of air by absorption or other means. A total lobular plug in normal communication with free adjacent lobules has not been seen to result in atelectasis, and this consideration appears to explain the failure of atelectasis formation in lobe *B*, figure 5, as well as many of the other failures in our work to obtain this condition after bronchial obstruction.

No explanation, however, has yet been obtained for the marked accelerating influence of straining respiration on atelectasis formation. In addition, there remain unexplained the marked differences in the rate of atelectasis formation that are to be seen when both the position of the obstruction and the type of respiration are kept constant. There must be important factors still unrecognized which enter into the pathogenesis of the condition, in one instance to speed absorption of air and in another greatly to delay or to stop it. Since absorption of air is by the blood stream,<sup>10</sup> these factors probably relate to that, and improvement in the circulation or its retardation would be expected to hasten or to slow absorption of air. Investigations along this line are under way.

## CLINICAL APPLICATION

We have no additions to make to the measures of prevention and treatment already in practice. However, these deserve discussion as to advisability, with reference to the principles of bronchial obstruction and atelectasis formation already explained. Another circumstance of great importance requires attention—the infection that precedes and accompanies atelectasis in most instances. Bacterial or chemical inflammation of the bronchi is usually responsible for obstructing secretions and exudates, and to infection are due in large part the distressing symptoms and dangerous complications of atelectasis. That the dyspnea, fever and prostration are immediately related to the infection rather than to collapse of the lungs, is strongly suggested by the facts that compressive atelectasis, as in pneumothorax produces relatively slight cardiorespiratory disturbance and no toxemia, and that obstructive atelectasis in the dog does not give rise regularly to any of these effects. The loss of function of so much lung is probably unimportant in itself in most cases. Attention has been directed in the recent literature to the complications of atelectasis and particularly to pneumoma. While there is no direct and convincing evidence<sup>20</sup> that atelectasis represents the first stage of pneumonia, or even that it predisposes to pneumonia, there is little doubt that the serious bronchitis that leads to massive atelectasis may readily progress to pneumonia.

In applying to clinical use the knowledge of atelectasis that has been gained, caution is advisable lest by active intervention, calculated to be beneficial in one respect, actual harm is done by transgression of principles not yet understood. Care should be taken also not to aggravate the accompanying infection. Indeed, conservatism may well be indulged in for the present, as atelectasis in massive proportions is unusual, its morbidity brief and fatality from the condition itself rare.

For preventing the accumulation of inflammatory products in the bronchial tree, recourse may be had to medication and to encouragement of natural forces for elimination from the bronchi. Inhibition by drugs of the mucous secretions is indicated in nonbacterial irritations of the tract, as in inhalation anesthesia, and it has little place, if any, in well developed infectious bronchitis. Inhalation of steam is beneficial in moistening and warming the inflamed surfaces. Of the eliminative forces, the ciliary and peristaltic functions may be aided by attention to their two main impediments—i.e., the suction that follows absorption of air distal to a total obstruction, and adverse gravitation. Fluids

<sup>20</sup> The hypothesis advanced by Corvillo and his associates designating atelectasis as a constant precursor and disposer to pneumonia as yet lacks any direct anatomicopathologic proof. They have demonstrated no more than the frequent juxtaposition of the two conditions.

accumulating in the bronchial tree tend to settle first of all in the smaller passages, and the earliest total obstruction is likely to be lobular. At this stage it should be possible to prevent collapse of the lung in the obstructed parts by maintaining aeration of the free portions of the lobe and permitting intercommunication at the periphery. This may be done by means of an occasional deep breath. Even after isolation of the part has become complete, as in lobular obstruction, deep breathing may still be effective, since the plug in one or another of the passages may be of small size and admit air by inspiratory dilatation of the bronchus, by thinning and rupture at the center or by being sucked into the periphery and leaving some of the small branches free. Here again, it should be appreciated that an occasional deep breath or two is sufficient. Continuous hyperpnea, as induced by inhalations of carbon dioxide,<sup>21</sup> is probably unnecessary and may be tiring. The added muscular exertion called forth, reflex and subtle though it may be, must require output of energy. As a matter of fact, when massive obstruction has been reached dyspnea and cyanosis (high carbon dioxide content of the blood) are often already at hand and require no augmentation. The impediment to the eliminative functions by gravitation is, of course, readily replaced by equally effective assistance from that source, by placing the patient's head at a level below the bases of the lungs. Coughing should be used in moderation, since its action is not always effective and may be harmful. The chief benefit from the cough is to be expected in the removal of partial obstructions, and the action becomes uncertain in total obstructions. The ciliary and peristaltic forces are mainly to be relied on in the latter condition. On the other hand, it is clear that coughing has a somewhat irritating effect and, in addition, tends to accelerate the absorption of air that is imprisoned in the lung. Excessive spontaneous coughing should be controlled. It must be remembered that rest is important to the general resistance of the patient in combating the coincident infection.

The following plan of procedure is suggested for routine use in preventing the development of bronchial occlusion.

Elevation of the foot of the bed is the only constant addition to the ordinary nursing and general supportive measures. If it is evident that bronchial secretions are excessive a regular schedule is adopted with a change of side in the lying position and with encouragement to inspire deeply and to cough once or twice. Hourly or half-hourly intervals are used. When suggestion is not effective or desirable to obtain the inspiration and cough, as in sleeping, unconscious or otherwise uncooperative patients inhalations of carbon dioxide should be

<sup>21</sup> Henderson, Haggard, Corvillo, Birnbaum and Radloff (footnote 16 fourth reference.)

substituted. Breathing of steam is used if specially indicated. Sedatives are administered freely and in amounts to control spontaneous coughing that occurs in excess, and to obtain rest.

Once physical signs and symptoms indicate that atelectasis has occurred, suction is operating to draw the offending plug toward the periphery, and all forces of expulsion are at a disadvantage, particularly that of cough. Also, any straining in breathing acts to accelerate absorption of the pent-up air that still remains, and respiratory exercises that contain this element are to be minimized.<sup>22</sup> The effects of air hunger and toxemia are also added to the picture. Bronchoscopic aspiration of the obstructing material has been demonstrated to have a place in the treatment for this condition, for in numerous reported cases<sup>23</sup> the atelectatic lung has returned to a normal roentgenologic appearance and the symptoms have disappeared after the removal of mucus from the bronchi. There is usually an immediate aeration of a part of the lesion, and the remainder then becomes air-containing section by section. Relapse may occur at any stage. It is often impossible to unburden all the branches of a lobe by aspiration, nor is that necessary. The steplike aeration described is probably due to a progressive process of inflation through the periphery from one respiratory unit to the next. Thus, after bronchoscopic treatment and liberation of one or two branches the patient immediately inspires into and aerates the corresponding part of the lobe. From this, in turn, the air may be inspired by way of peripheral communications into adjacent portions that are still obstructed. This serves to inflate the parenchyma lying distal to the remaining bronchial plugs, to relieve the suction and to provide available air for the action of cough, clearance of the rest of the obstruction proceeds spontaneously by cough. It should be emphasized, however, that bronchoscopy in other than highly skilful hands may add materially to the acute tracheobronchitis and bring about more damage than benefit. The rate of bronchial secretion may be accelerated and relapse encouraged thereby, cases are on record that required repeated bronchoscopic intervention. It then becomes a question whether the patient is afforded greater peace and security from the intermittent engagements with the endoscopist than he would be if allowed to pursue the natural course of the condition under conservative management.

The routine treatment for atelectasis may be planned to follow the same measures that have been suggested for prevention.

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<sup>22</sup> Attention is called to the fact that deep breathing has not been found to fall into the category of straining respiration, unless there is resistance to expiration as in coughing, grunting, moaning, etc.

<sup>23</sup> Lee, W. Work ready for publication.

### SUMMARY

The present understanding of the pathogenesis and clinical management of obstructive pulmonary atelectasis is reviewed to set forth certain problems

- 1 The inconstant action of cough and other natural eliminative forces in maintaining and effecting clearance of the lower respiratory passages

- 2 The uncertainty of incidence of atelectasis formation after bronchial obstruction

- 3 Irregularity of the rate of atelectasis formation

Solution is offered for some of these problems by reference to certain principles of respiratory function recently determined

- 1 Exchange of air between parts of a lobe at the periphery

- 2 The accelerating influence of straining respiration on the rate of absorption of air in the occluded part of the lung

- 3 The dependence of cough for its eliminative effect on the presence of available air in the occluded part of the lung

It is pointed out that the third problem, which concerns the rate of atelectasis formation, remains partly unsolved

Evaluation is made of the methods in vogue for the prevention and treatment of atelectasis

# ALVEOLAR GAS EXCHANGES AND ATELECTASIS

## THE MECHANISM OF GAS ABSORPTION IN BRONCHIAL OBSTRUCTION \*

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### Physiology

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Solubility, Diffusion and Osmosis

Solubility Coefficient

Diffusion Pressure

Osmotic Pressure

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The Regulation of Respiration and Circulation

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#### Our Theory of Production of Atelectasis

#### Comment

#### Conclusion

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In previous papers we have endeavored to present clinical and experimental evidence in favor of the theory that atelectasis is always produced by complete bronchial obstruction including those cases in which it follows collapse of the lung from compression as in open or tension pneumothorax or abundant pleural effusion.

If we have repeatedly and persistently dealt with this subject it is because we consider that it is of greatest practical importance that atelectasis should be associated in the mind of the practitioner with bronchial obstruction and that he should seek out its cause by further investigation of the bronchial tree. We believe that he must accept as an axiom that whatever may be the conditions favoring the production of atelectasis—impairment of pulmonary ventilation, narcotics, postoperative splinting of the thoracic cavity because of pain, posture, decrease of cough because of narcotics or pain, previous common colds, etc.—there is but one immediate cause, complete bronchial obstruction. Roentgenographic and often bronchoscopic examinations are necessary to establish the particular cause of the disease in a given case. To cite only a few examples, many latent foreign bodies, tumors of the mediastinum and more particularly many tumors of the lung (which in a great majority of cases are of bronchogenous origin) might be discovered in this way. It is obviously desirable to diagnose such tumors in their earliest stages when they are still operable. Then again in the cases of nonopaque foreign bodies in children, in prolonged forms of postoperative atelectasis and even in hemoptysis with sudden symptoms of impending asphyxia, a knowledge of the obstructive nature of atelectasis would be of the greatest importance for the initiation of appropriate treatment. Last but not least, with the idea of the relation between bronchial obstruction and atelectasis always in mind, the thoracic surgeon in carrying out collapse therapy or resection of a lung for chronic suppuration of the organ will adopt preventive measures or will have always at hand the necessary instrumentarium for treating bronchial obstruction due to pus expressed from the collapsed lung. Many fatalities after chest operations believed due to postoperative shock are simply due to obstructive atelectasis, as is clearly shown by a careful perusal of case histories cited in the literature (Berry and Lambert). It is only reasonable to suppose that a good number of these deaths might have been prevented even after such an accident had happened. Had the necessary measures been known and readily available, advantage could have been taken of that short period which intervenes between the moribund state of the patient and death for reestablishment of respiration. So long, however, as we content ourselves with such hazy explanations as 'vasomotor reflex,' 'bronchomotor reflex,' or 'angioneurotic edema,' no real effort will be made to avoid or treat the real and tangible cause of atelectasis, which we repeat is bronchial obstruction.



Obstructive atelectasis or apneumatoxis of the lung is generally admitted to be produced by absorption by the circulating blood of the air entrapped in the alveoli. Lichtheim gave an experimental demonstration of this fact in 1879 by plugging the bronchi of rabbits with laminae of spongewood and noticing the absorption of air. Furthermore, he showed that oxygen is absorbed much more quickly than air. This theory is, of course, not upheld by those authors who believe in the mechanical expulsion of alveolar air by capillary engorgement (vasomotor reflex theory) or edema of the alveoli (angioneurotic edema).

More recently, Rappaport (November, 1929) completely rejected the theory of the absorption of alveolar gas by the blood. He endeavored to explain the production of obstructive atelectasis by a mechanism of "respiratory decompensation" leading to a "plethora of the lung." "Failure in function of one lung," he said, "results in the production of excessive plethora which finally floods the air passages and produces atelectasis."

The mechanism of production of atelectasis is either failing respiratory function by way of direct immobilization or by way of excessive compensation, which fails. He added, "As to the bronchial plug theory, I think it is untenable, that it is not even worth discussion." Bronchial obstruction causes only bronchial emphysema.

the conception of absorption of the air behind the plug is all wrong. For the foregoing statements, this author offers no experimental proof. "I have no such evidence," he said, "mine is purely clinical."

On the other hand, Van Allen and Adams, in a recent (February, 1930) purely experimental paper, arrived at the following conclusions:

1 Even complete bronchial obstruction does not lead to atelectasis in the normal lung if the animal breathes quietly, straining respiration is essential to the production of atelectasis.

2 Pent up bronchial air is "probably" lost from the lung by absorption by the blood stream. "It is a curious circumstance," said these authors, "that air which is imprisoned within the normal lung under conditions of quiet respiration remains without absorption for a long time if indeed, it is ever absorbed, whereas air introduced into the neighboring pleural cavity or into the tissue spaces elsewhere tends quickly to disappear. Perhaps the query is more pertinent as to why air, and especially the nitrogenous part of it, at any point should be absorbed." In the experiments, however, in which these authors plugged the bronchus leading to the lower right and to the accessory lobes but the lobe only was ligated the pulmonary artery leading to the accessory lobe was deflated and atelectatic whereas the accessory lobe (the pulmonary artery of which was ligated) "was air-containing and of normal appearance."

ance" This seems, to us, characteristic evidence of the production of atelectasis by absorption of the alveolar air by the circulatory blood, because only in this way the necessity of circulatory integrity in its production would be understood Van Allen and Adams do not discard the theory of alveolar gas absorption, but, on the other hand, they do not definitely admit it because of the apparent difficulty with this theory to explain their failure to produce atelectasis in quiet respiration They therefore compromise "Those experiments," they said, "designed to test the part played by the blood stream in atelectasis formation, must be guarded as to interpretation In ligating the vessels the nerves to the lung may also have been injured, and the failure of an absorption under these circumstances may have been due to either or both of these effects"

We have quoted from these two papers because they represent, so to speak, the extreme wings of the series of papers on atelectasis published during the last two years both in America and abroad, which cast doubt on the mechanism of production of this disease by bronchial obstruction and absorption of the alveolar gases by the blood The first is a purely clinical paper without any attempt at experimental verification of the statements and theories advanced The second is purely experimental Both, however, have one point in common They express doubt as to absorption of alveolar air by the blood circulating in the alveolar capillaries It would seem that the solution to the whole question lies in the answer to this question Is the alveolar air absorbed by the blood and if it is, what is the mechanism of this process? It is obvious that the answer to the question and the solution of the problem will be necessary to establish the obstruction theory on a solid and indisputable physiologic basis, but once this proof has been given, we feel that the other theories usually advanced would be dealt a definite blow and should be discarded

The rationale for determining the exchange of gases in the lung in relation to atelectasis is thus apparent The task was difficult, complicated and full of pitfalls It required a great deal of specific knowledge and complicated experimentation, of extreme precision in the quantitative determination and many precautions and continuous check-ups in the interpretation of the results obtained The experiments were long often lasting twelve, fifteen, twenty or even forty-six hours, during which time many details required coordination and constant supervision, among these details were the occluding balloon the pleural cannulas the roentgen apparatus, the oscillating vacuum source the manometers and recording devices etc During these long hours the animals were put to the hard test of deep narcosis and intrabronchial manipulation We had to face many disappointments in order to "carry

on" for over a year. On the other hand, the problem was so captivating and the results obtained of such great interest that no effort seemed too great.

We feel that the data to be presented definitely uphold the production of atelectasis by complete bronchial obstruction and absorption of the alveolar air, and that they can explain the pathogenesis of this disease without the additional help of "straining respiration," "valvular expulsion," "respiratory decompensation," or "respiratory failure" (with or without "lung plethora"), "angioneurotic edema," "vasomotor reflex," etc.

#### PHYSIOLOGY

Since our problem is based entirely on physiologic grounds and in close relation to the physics and chemistry of respiration and the exchange of respiratory gases, it is necessary for a full comprehension of the underlying details, to make some ingress into the fascinating but also often desperately complicated question of respiration. Modern conceptions on respiration have modified the older theories in many ways. On the other hand, in the painstaking work of many of the older physiologists, especially of Pflüger, Ludwig and their pupils, we found much relevant material precious to our own work. The prominent controversy concerning the function of the alveolar respiratory membrane lasted for over fifty years, the last word on the subject has not yet been said. Is it a simple semipermeable membrane through which the exchange of gases proceeds according to the laws of diffusion as maintained by Pflüger, at the head of Bonn's laboratory, or is it a true secretory epithelium secreting oxygen much as salivary epithelium secretes saliva, as Ludwig and his pupils at the Leipzig Laboratory maintained? Many papers of great significance and accuracy were published during that heroic period of study on the respiration. Although almost completely forgotten today, they are in general accord with the fundamentals of the modern physiology of respiration. Among these older works and under titles apparently bearing no relation to our problem, we were indeed surprised to discover that bronchial obstruction was carried out previously on the dog (Wolffberg 1871) and even on man (Loewy and von Schroetter, 1905). The object of these authors was to determine the exact composition of the gases of the alveolar capillary blood by analyzing the entrapped alveolar air since in from five to fifteen minutes after bronchial obstruction an equilibrium sufficient for their purpose in gas percentages is established between the alveolar gases and the gases in the venous capillaries of the lung. Our results are in complete accord with those given by these authors as we shall later see.

*Requirements for the Exchange of Gases*—Respiration is the exchange of gases between alveolar air and venous alveolar blood on the one hand, and between the tissues, lymph and capillaries on the other hand. The exchange of gases in the lung—the only one which interests us at present—requires the following conditions: (1) the integrity of the endothelial membrane composed of the alveolar and capillary endothelium which separates the alveolar air from the venous capillaries of the lung, (2) the difference in partial pressures of the gases present on either side of this membrane, (3) the integrity of pulmonary ventilation with the continuous renewal of the alveolar air which is only possible if there is no interference with the patency of the air passages from the larynx to the respiratory bronchioli, atria and ducti alveolaris, and (4) the integrity of the intrapulmonary circulation.

No one of these conditions can be altered without producing profound changes in the mechanism of the exchange of gases.

It is easy to understand how edema or inflammatory thickening of the alveolar membrane will impair or stop this exchange. Likewise an unhampered circulation is essential for the normal exchange of gases. The blood being the normal and only gas carrier in the organism from the lungs to tissues and vice versa, it is obvious that impairment or interruption of the pulmonary circulation will preclude or bar completely the usual exchange of gases. Likewise, an efficient ventilation is just as essential. It is the *sine qua non* condition for maintaining the gases on either side of the alveolar membrane under those conditions of different partial pressures which are absolutely essential for the exchange of gases. In fact, the most important factor in the accomplishment and regulation of the exchange of gases is the difference in partial pressures of the gases in the alveolar air and in the venous alveolar capillaries.

As Paul Bert first showed, it is not the total pressure of the gas mixture but the partial pressure of each individual gas, each acting as if it were alone, which is of importance in physiology. In a mixture of gases when no chemical action occurs each gas behaves independently. Dalton has shown this fact and formulated the law of partial pressures which bears his name. Thus if 100 cc of oxygen and 400 cc of nitrogen both at one atmosphere of pressure are mixed the resulting mass of gas occupies 500 cc at the same pressure, but the oxygen acts as if it were under a pressure of only one fifth of an atmosphere ( $\frac{1}{5} \times 760 = 152$  mm of mercury) while the nitrogen acts as if it were under a pressure of four fifths of an atmosphere ( $\frac{4}{5} \times 760 = 608$  mm of mercury).

*Solubility, Diffusion and Osmosis*<sup>1</sup>.—We shall be obliged to use physiochemical terms such as solubility coefficient, diffusion and osmotic pressures, etc. A short explanation of these terms will therefore be useful.

*Solubility Coefficient*.—Solubility of a gas in a liquid depends on the nature of the gas, the nature of the solvent, its pressure and the temperature. The solubility of hydrogen, oxygen, carbon dioxide in 1 cc of water at 15 C and at 760 mm of mercury pressure are hydrogen, 0.019, oxygen, 0.0342, and carbon dioxide, 1.002. The solubility of the different gases is not the same in different solvents, but the order of solubility of gases in different liquids is almost always the same.

The solubility of a gas in a given solvent, such as water, is appreciably diminished by the presence of dissolved solids or liquids, especially electrolytes. According to Philip, the presence of solids diminishes the solubility of gases because a part of water enters into combination with the solute and is thus made unavailable for absorbing the gas. Solubility of a gas increases with increased pressure and decreases with elevation of temperature. Furthermore, concerning the nature of the gases, those which present basic or acid reactions are much more soluble than the neutral ones as, for example, the case of carbon dioxide compared to nitrogen. But the predominant factor in the solubility of a gas is, again, pressure. According to Henry's law "The weight of a gas dissolved in a liquid is proportional to the pressure of the gas." One should not, however, confuse "weight" and "volume." Since volume and pressure at a constant temperature are inversely proportional (Boyle's law), the law of Henry may be stated thus "The volume of a gas absorbed by a given volume of liquid is independent of the pressure," but the weight of the gas absorbed is, of course, proportionately increased. Dalton has shown that the solubility of individual gases in a mixture of gases, is directly proportional to their partial pressures, the solubility of each gas being independent of the pressure of the others.

From these considerations, it follows that the concentration of the dissolved gas is directly proportional to the concentration of the gas in the free space above the liquid. In fact, when a definite volume of liquid is saturated with a gas at a constant temperature and pressure, a condition of equilibrium is established between the gas in solution and that over the solution. If  $C_1$  represents a concentration of gas in the liquid, and  $C_2$  the concentration in the free space, we have the equation  $\frac{C_1}{C_2} = K$ , where  $K$  represents the solubility coefficient.

<sup>1</sup> An excellent summary of the physiochemical aspects of the question will be found in Getman's "Outlines of Theoretical Chemistry," ed 4 New York John Wiley & Sons, 1928.

*Diffusion Pressure*—If a cylinder containing hydrogen is placed mouth to mouth on a cylinder containing oxygen, although hydrogen is sixteen times lighter than oxygen after a short while we shall find a perfect mixture of the two gases. Hydrogen has diffused against the laws of gravity into the oxygen.

If a few cubic centimeters of a concentrated solution of cane sugar is placed in the bottom of a tall cylinder and water is added, care being taken to prevent mixture, the sugar immediately begins to diffuse into the water, until the concentration of sugar is the same throughout the liquid. The sugar molecules move from a region of high concentration to a region of low concentration and diffuse into the water.

In the case of gases the rate of diffusion is extremely rapid. For the hydrogen molecule this speed is 1840 meters per second or faster than a rifle bullet. The average speed for oxygen under the same condition is one fourth of this value or 460 meters per second. Thus the "rate of diffusion of gases is inversely proportional to the square root of the density of the gas."

In solution the process of diffusion is much slower. But the molecules obey the same fundamental laws, and they are explained in the light of the same theory—the molecular kinetic theory. If the solution and the pure solvent are separated by a semipermeable membrane which is permeable to the solvent and not to the solute molecule, the latter will exert a pressure on the membrane as a result of their successive impacts on it. In dilute solutions "the diffusion pressure" follows the gas laws.

*Osmotic Pressure*—Osmosis is the diffusion of a liquid through a membrane. When a salt solution, for example, is separated from water by a suitable animal membrane, the water diffuses through the membrane more rapidly than the salt. The level of the salt solution rises causing an appreciable hydrostatic pressure to develop. Since this pressure is caused by the process of osmosis it is called the "osmotic pressure."

The osmotic pressure of a solution is not to be regarded as an actual pressure exerted by a component of the solution (solvent or solute) but rather as the difference in pressure which must be established between the solution and solvent, respectively, in order to render the escaping tendency of the solvent equal to that of the solution. According to the molecular kinetic theory, if pure water is placed on both sides of a semipermeable membrane which allows the passage of the solvent only but not of the solute, the molecules of water being in ceaseless motion will bombard the membrane from both sides. But when the molecular concentration (number of molecules in a unit of space) on both sides is the same it is obvious that as many molecules will pass through the

membrane in one direction as in the other and that no osmotic pressure will develop

If now, instead of pure water a solution is placed on one side of the semipermeable membrane, it is obvious that the number of molecules of water present in it in a unit of volume is less than in the pure solvent. Under these new conditions, the number of molecules of solvent passing through the membrane in a unit of time will be less for the solution than for the pure solvent. Thus the equilibrium is disturbed in favor of the pure solvent and this difference in pressures constitutes the osmotic pressure. On the other hand the molecules of the solute tend to diffuse into the pure solvent. But as the molecules of the solute cannot pass through the semipermeable membrane, a pressure develops which represents the diffusion pressure of this particular substance.

It is interesting to point out here that equimolecular quantities of different substances dissolved in equal volumes of the same solvent exert the same osmotic pressure and produce the same relative lowering of

TABLE 1—*Osmotic Pressure of Cane Sugar Solutions*

C	P	$\frac{P}{C}$
1	53.5	53.5
2	101.6	50.8
4	208.2	52.0
6	307.5	51.2

vapor pressure. Since equimolecular quantities of different substances contain the same number of molecules, it is evident that the magnitudes of osmotic pressures and relative lowering of vapor pressures are dependent on the number of dissolved units present in the solution and are independent of the nature. In the same way, Pfeffer showed that the osmotic pressures increase with the concentration to which they are proportional. In table 1, C denotes the concentration of the solution, P the corresponding osmotic pressure expressed in cubic centimeters of mercury, and  $\frac{P}{C}$  the ratio of osmotic pressure to concentration.

It is clear from the figures in table 1 that the osmotic pressure is proportional to the concentration of the solution since  $\frac{P}{C}$  is approximately constant. The osmotic pressure exerted by any substance in solution is the same as it would exert if it were present as a gas in the same volume as that occupied by the solution.

We have gone rather extensively into the question of osmotic pressure because it is desirable to show that diffusion or osmotic pressures are not small forces as might easily be believed. They represent tremendous energies, for we have seen that the diffusion rate of hydrogen exceeds the speed of a rifle bullet and, as shown in table 1 the osmotic pressure

of a 6 per cent cane sugar solution is equal to 307.5 cm. of mercury that is, over 4 atmospheres. It is really marvelous how these forces act in our organism in such a smooth and coordinated way.

The surface of the human lungs according to Zuntz, is 90 square meters or about 1,000 square feet. During quiet breathing 300 cc. of oxygen and about the same quantity of carbon dioxide diffuse through in one minute. If the whole surface were used for diffusion the amount of gas passing per minute through 1 square centimeter would be only 0.0003 cm. and could be accomplished according to Fick with a partial pressure of only 1 mm. of mercury.

It is necessary, however, to remark here that the velocity of diffusion is not only inversely proportional to the square root of its density as we have previously said but also that it is proportional to the coefficient of solubility of the gas in the fluid concerned. That is why the speed of diffusion of carbon dioxide through a wet membrane is thirty times greater than for oxygen, although its density is greater. This can be easily shown by tying closed a frog's lung filled with oxygen or atmosphere and placing it in an atmosphere of carbon dioxide. Within a minute the lung is distended owing to the diffusion of carbon dioxide into it, for the coefficient of solubility of carbon dioxide is thirty times greater than that of oxygen.

Oxygen and carbon dioxide are not merely dissolved in the plasma of the blood. The bulk of oxygen and carbon dioxide is in chemical combination in the blood. The first combines with hemoglobin, the second with alkali.

*The Dissociation Curve of Hemoglobin in Relation to Respiration* — The oxygen-hemoglobin compound has the property of disassociating with a fall in the partial pressure of oxygen, this dissociation is complete when the oxygen pressure is reduced to zero. In this way hemoglobin represents an oxygen reserve in the red cells which maintains constant the amount of oxygen dissolved in the plasma, the latter representing the vapor-pressure above an oxygen solution.

Besides the partial pressure of oxygen in the alveolar air or tissues, another important factor in the dissociation of oxy-hemoglobin is carbon dioxide. Increase in carbon dioxide hastens the dissociation of oxygen, it "shifts the dissociation curve of oxy-hemoglobin to the right" and thus facilitates the unloading of oxygen into the tissues as the carbon dioxide in the blood increases. Although this is strictly correct it is, according to Haldane, of much less importance than the shifting of the carbon dioxide absorption curve in consequence of the reduction of hemoglobin.

In fact decrease of oxygen in the blood and hemoglobin unsaturation increase the capacity of the blood for carbon dioxide probably



because reduced hemoglobin is a more alkaline substance than oxygen-saturated hemoglobin. The latter acting as a weak acid keeps carbon dioxide out of combination with alkali. Whatever the cause of this action may be, it is certain that saturation of hemoglobin decreases the capacity of blood for carbon dioxide the result being that with high oxygenation the partial pressure of carbon dioxide in the blood rises although its percentage remains the same. For this reason more carbon dioxide is given off by the blood when its oxygen saturation is high (Werigo, Bohm and Halberstadt). Now it follows that if one lung is ventilated with a neutral gas as nitrogen and the other with air, the latter will give off nearly 50 per cent more carbon dioxide than the former.

Decrease in carbon dioxide has another important result, discovered by Bohr (1904) and called the "Bohr effect." Such a decrease shifts the dissociation curve of hemoglobin to the left so that whereas in the venous blood (carbon dioxide, 45 mm of mercury, oxygen, 40 mm of mercury) the hemoglobin is 68 per cent saturated, if carbon dioxide falls to 10 mm of mercury the hemoglobin (without any increase in the oxygen pressure) becomes 85 per cent saturated. Furthermore, the oxygen is more firmly held in combination with hemoglobin so that notwithstanding this apparent increase in oxygen pressure and absence of cyanosis, the oxygen available to the tissues is greatly diminished.

*The Regulation of Respiration and Circulation*—In a previous paper on "Circulation in the Consolidated Lung," we stressed the point of perfect parallelism between ventilation of the lung and its circulation. We showed by injecting the pulmonary artery in the living animal with iodized poppy seed oil 40 per cent and the capillaries with India ink in Ringer's solution, that atelectasis as well as other varieties of pulmonary consolidation are accompanied by shrinkage of the alveoli and by shrinkage and collapse of the alveolar capillaries. Not only do these two processes advance hand in hand, but they are also reversible, collapse of the alveolar capillaries following ligature of the pulmonary artery produces shrinkage of the alveoli which ultimately leads to atelectasis and inflation of the lung increases blood flow through the lung. The question that interests us now is how this regulation occurs and by what mechanism this synchronism is insured.

"At bottom," said Haldane "the regulation of the circulation is a chemical regulation, just as in the case of breathing." Circulation and respiration are regulated by the metabolic requirements of the tissues which requirements in the last analysis are represented by the partial tensions of oxygen and carbon dioxide or more exactly, by the hydrogen ion concentration in the tissues. Circulation seems to be so regulated as to keep the pressures of oxygen and carbon dioxide approximately

steady in the venous blood of any particular origin. During muscular work, for instance, where a rise of carbon dioxide and fall of oxygen pressure is produced, an increase in blood flow through the muscles follows, with a corresponding increase in venous blood pressure (Henderson and Haggard, 1918). Krogh has shown that under resting conditions the great majority of capillaries in muscular tissue are contracted and impermeable to blood, so that neither blood corpuscles nor the finest particles of india ink can pass through them. Nor is the full arterial blood pressure capable of forcing them open. Whenever the tissue is stimulated to activity, however, these capillaries open wide so that blood can pass through them freely. "It seems that increased oxygen and carbon dioxide production with increased hydrogen ion concentration is the natural stimulus bringing about an increase in local circulation, the regulation of the respective oxygen and carbon dioxide pressures disturbed by the increased activity of the muscles is thus brought about." Once the fundamental fact is grasped, said Haldane, that the general flow of blood throughout the body is correlated with gas pressures in the capillaries, the whole physiology of the circulation appears in a new light. "In fact, so long as the contractions of the ventricles are complete the volume of blood discharged at each beat must depend on the extent to which the right ventricle fills in diastole. This in turn depends on the rate at which blood is let through from the arteries to the veins. It is therefore the rate at which the systemic blood is allowed to pass through the tissues into the venous system that determines the amount of blood pumped by the heart, and as already pointed out, the rate at which blood is allowed to pass through the tissues is determined by their metabolic requirements. It is evident that in this regulation by both the heart and the blood vessels the nervous system plays an important part, just as in the case of regulation of breathing, but the main fact must never be lost sight of, namely, that the primary factor determining the rate of circulation is neither the heart nor the nervous centers, but the metabolic activities of the tissues. This is exactly what Claude Bernard meant when he said in his "*Leçons sur les phénomènes de la vie*" that "all the vital mechanisms, varied as they are, have only one object, that of preserving constant the conditions of life in the internal environment" (the blood).

Henderson and Haggard in a series of papers on "Acapnia and Shock," showed that a condition can be brought about in animals by excessive ventilation of the lungs which washes out the carbon dioxide and produces a state of alkalosis with slowing of the circulation and consequent great anoxemia. The slowing of the circulation tends, as Haldane remarked to "diminish the alkalosis in the tissues but only at the expense of producing most formidable anoxemia."

Anoxemia and alkalosis persist, and shock is produced as the circulation rate decreases and the heart fails

However, the condition of shock might be produced by an altogether different mechanism, especially in postanesthetic conditions. In these cases as Van Slyke, Van Slyke Austin and Gullen, Ronzoni, Leake and others have shown, instead of an alkalosis as in apnea, there is always a more or less pronounced degree of acidosis with decrease in alkali reserve, a decreased partial pressure of carbon dioxide in the alveolar air and an increased hydrogen ion concentration (low  $p_H$ ). This condition, which is similar to the condition frequently observed in cases of nephritis and diabetes due to nonvolatile acids, has been described by Hasselbach and Gammeltoft as "uncompensated acidosis" and by Van Slyke as "uncompensated alkali deficit". The carbon dioxide (in the form of carbonic acid) is high and not decreased in proportion to the fall of blood bicarbonate. As Leake and Henderson pointed out, it seems extremely plausible that this acidosis might be due to defective sugar oxidation. "Among the essential factors of an efficient oxidation of sugar are: Adequate supply of sugar, an ample supply of oxygen and sufficient insulin to facilitate the process. Deficiency in any of these factors leads to withdrawal of alkali from the blood into the tissues. In the dynamic equilibrium of this process the mass action of oxygen is balanced against the mass action of bicarbonate ion and the hydrogen ion concentration is a variable dependent (through respiration) upon the ratio of oxygen to sodium bicarbonate and tending to restore that ratio to normal by the shift of alkali from blood to tissues and vice versa" (Henderson). There is thus a close parallelism between the percentage of oxygen and the amount of alkali in the blood which might explain how anoxemia can produce "uncompensated alkali deficit". It would therefore seem possible that between anoxemia and postoperative acidosis there exists a relation of cause and effect. It is not within the scope of this paper to enter into this topic which will be dealt with in a forthcoming paper. We only wish to point out here the relation existing between deficient sugar oxidation, acidosis, hypoventilation and postoperative pulmonary complications (atelectasis). It would seem not to be a mere coincidence that these complications are most frequently present after operation on the upper part of the abdomen, probably exposure of the liver, exhaustion of sugar reserves, disturbed insulin production and decreased ventilation have a part in their production. This condition of hypoventilation favors "respiratory stagnation" and leads to atelectasis by facilitating bronchial retention and obstruction and thus to the absorption of alveolar air by the venous blood circulating in the perialveolar capillaries.

In order to present all the elements necessary to the complete comprehension of this problem it is essential to deal with the composition of alveolar air and the gases of the venous blood

*Composition of the Alveolar Air*—The composition of the alveolar air, analyzed according to the method of Haldane and Priestley, can be considered, in normal persons at rest and at average barometric pressure, as follows: oxygen, 15 per cent, carbon dioxide, 5 per cent, nitrogen, 80 per cent (Haldane's figures are: carbon dioxide, 5.6 per cent, oxygen, 14.5 per cent). In order to simplify the question, we are going to consider 760 mm of mercury as the normal pressure in the lung. In reality, the alveolar air being saturated with water vapor, the actual gas pressure is  $760 - 47 = 713$  mm of mercury, 47 mm of mercury being the tension of water vapor, the effect of the negative intrapleural pressure (of from 5 to 8 mm of mercury) is negligible. Knowing the percentage of the different gases, we can easily calculate their respective partial tensions: oxygen is  $\frac{15}{100} \times 760 \text{ mm} = 114 \text{ mm}$  of mercury, carbon dioxide is  $\frac{5}{100} \times 760 \text{ mm} = 38 \text{ mm}$  of mercury, and nitrogen is  $\frac{80}{100} \times 760 \text{ mm} = 608 \text{ mm}$  of mercury.

It is understood that the foregoing figures are only approximate and represent composition of the air contained in the air sacs. From here toward the outside (atria, bronchiole, bronchi, trachea and larynx) the respiratory air approximates more and more the composition of atmosphere air, that is, oxygen, 20.95 per cent, carbon dioxide, 0.03 per cent, nitrogen, 79.02 per cent, so that in analyzing the expired air one finds it poorer in oxygen and richer in carbon dioxide as specimens are taken deeper in the lung. As one follows the gases from alveolar air and arterial blood to venous blood and to the lymph of the tissues the oxygen gradually decreases and the carbon dioxide increases.

The alveolar air is separated from the venous blood by the endothelium of the air sacs and of the capillary vessels which cover their external surface and by a negligible amount of extremely thin elastic and smooth fibers. In some species, as in birds, there intervenes only a vascular endothelium, because there is not a real respiratory epithelium but only a homogeneous hyaline membrane—an extremely thin film. Through this respiratory membrane the exchange of gases between alveolar air and the venous capillaries takes place.

*Venous Blood*—There is a great variation in the figures given by different authors in the composition of the gases contained in the venous blood in contrast to the figures for arterial blood which are remarkably constant. We shall use the figures given by Loewy and von Schloetter for man, to which the figures given by Henderson and Haldane approximately correspond: oxygen, 5 per cent, carbon dioxide, 6 per cent. These correspond to the following partial pressures

oxygen, 38 mm of mercury, and carbon dioxide, 45.6 mm of mercury. The partial pressure of nitrogen is the same as in the alveolar air, 608 mm of mercury, although its percentage is extremely low.

The question of gas pressures in the venous blood and more particularly in the venous capillaries of the lungs is of paramount importance. The exact determination of these pressures is not an easy task. Two methods are generally used. One is a direct analysis of the venous blood taken from the right ventricle, the other is an indirect determination by one of the following methods: the "hose method" of Haldane and Priestley or the "bronchial plugging" method of Siegfried Wolffberg. The latter, less well known and seldom reported, bears an important relation to our work. The rationale of this method is that if a bronchus is occluded, the air entrapped in it will after a while reach an equilibrium with the gases of the venous capillaries, so that a quantitative analysis of this air is equivalent to a gas analysis of the venous blood. Becher (1855) and F. W. Muller (1870) tried to realize this

TABLE 2—Results of Gas Analysis (Wolffberg)

Duration of Obstruction of the Bronchus, Minutes	Amount of Gases in the Alveolar Air, 100 Vol. of Gas	
	Carbon Dioxide	Oxygen
10	17	43
20	19	31
50	38	30
65	42	27

equilibrium by the voluntary holding of respiration. But, as Donders remarked, a short suspension of respiration is not sufficient to establish an equilibrium between alveolar air and blood gases, whereas, on the other hand, a prolonged cessation will cause an increase of carbon dioxide in the blood. We shall give a detailed description of the method of Wolffberg which is similar to ours, although used for a different objective. Loewy and von Schroetter applied a similar method to man (1905).

Wolffberg, working in Pflüger's laboratory (1871), used the lung catheter of Pflüger (fig. 1). With this catheter he was able to obstruct a bronchus for a time varying from three to ten minutes. He introduced this catheter in the trachea of dogs, previously tracheotomized without anesthesia. The terminal balloon of the catheter was then inflated, thus plugging the chosen bronchus, but through the central tube of the catheter the investigator was connected with the alveolar air and was able to draw a specimen of air for analysis. His method and results are extremely significant. We give his results in table 2.

The figures in table 2 show clearly that carbon dioxide increases and oxygen diminishes proportionately to the duration of occlusion until an

approximate equilibrium is obtained, at which time the composition of the venous capillary blood can be deduced from the percentages of gases present in the obstructed lung

The same question was studied in a similar way by Loewy and von Schroetter in a truly monumental work on respiration. These authors experimented directly on human beings by producing a temporary obstruction of a bronchus. The determination of the exact tension of gases in the alveoli and after a bronchial obstruction sufficiently prolonged to establish an approximate equilibrium of gas between alveoli and blood enabled them to calculate the amount of oxygen carried by the arterial blood and the amount of oxygen utilized in the organism, the

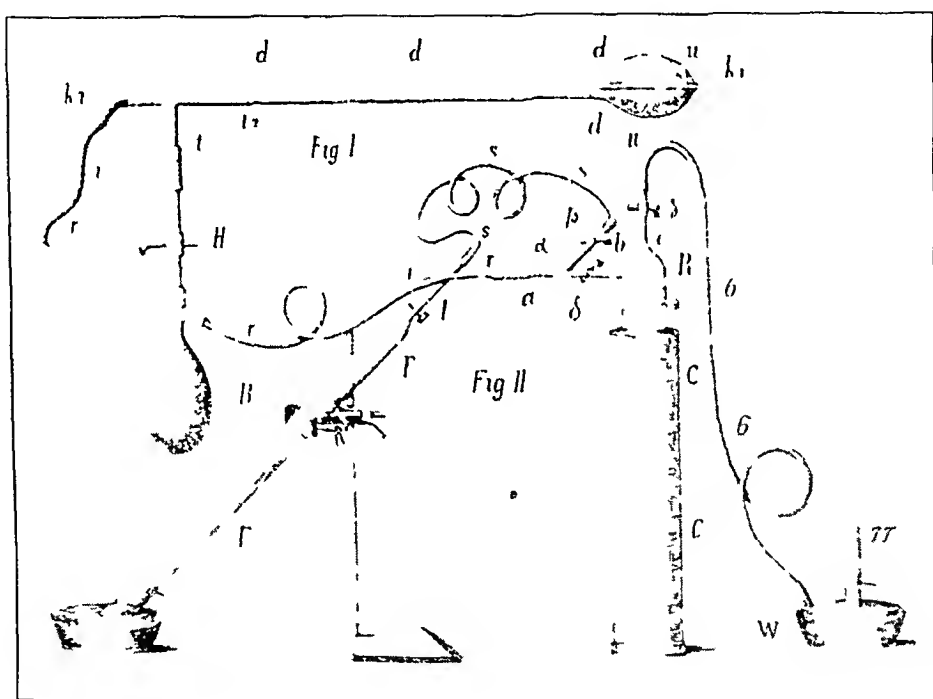


Fig 1—Pflüger's lung catheter (fig I) and gas analysis apparatus (fig II), used by Wolffberg for bronchial obstruction and analysis of the entrapped alveolar air. The catheter is composed of an elastic tube, *dddd*, which terminates in an elastic balloon, *uu*. This catheter is known in obstetrics as the Tarnier catheter used for inducing premature labor. At the end of the catheter a glass T tube (*t2*) was introduced, the vertical branch of which (*t1*) was connected with a rubber bulb (*B*) which could be separated from the catheter by a stop-cock (*H*). A fine glass tube, *k1k2* is introduced through the horizontal branch of the glass tube into the catheter and the balloon (*u*) at the tip of which a hole is made through which the tube can pass to the outside. The posterior half of the horizontal branch of the T tube is filled with cement around the fine glass tube, so that the latter leads from the entrapped alveolar air to the outside, once the catheter is introduced in a bronchus and the balloon (*u*) inflated, samples of air can be taken for analysis.

blood velocity, the heart output and finally the work of the heart. Their technic consisted in introducing into the trachea of the patients a special obstructive apparatus similar to the lung catheter of Wolffberg (fig 2). Its introduction was accomplished through the tracheal fistula in tracheotomized patients, or in other patients, through the mouth by means of the bronchoscope, using local anesthesia with cocaine applied to the laryngotracheal mucosa as in the usual bronchoscopy. Their catheter was composed of two silver tubes 1.5 and 0.7 mm in diameter, fixed together to allow an easy passage through the glottis or through a tracheal fistula. At the distal end an elastic balloon was attached in

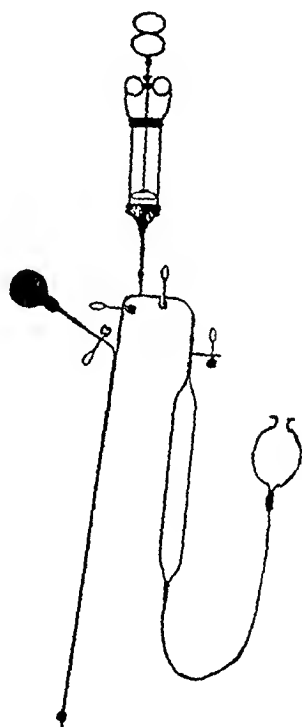


Fig 2—Lung catheter of Loewy and von Schroetter. On the left side is the catheter, with the terminal balloon, it is a double metal tube one tube being connected to the balloon and the insufflating bulb and the other with the entrapped alveolar air on the one hand, and with the apparatus for taking gas specimens, figured in the right side of the picture, on the other. Between them is adapted a syringe for aspirating the entrapped air and sending it into the gas-sampling apparatus (from Loewy and von Schroetter).

such a manner that it could be insufflated through the smaller of the tubes, whereas the other (larger) tube was terminated below the balloon and it was in communication with the pulmonary air below the obstruction. The other end of this tube was connected with a rubber tube, closed by a stop cock from which samples of air could be drawn by a syringe from the occluded lung for analysis. The oral end of the small tube was connected with an insufflating bulb for inflation of the

bronchial balloon Both tubes could be passed in an air-tight manner through a T form mouth valve (somewhat similar to that used in basal metabolism) which was connected with a spirometer and an inspiratory valve for measuring the expired air coming from the nonplugged lung (figs 3 and 4)

For the introduction the authors used the following technic The right bronchus was always used because of its more vertical direction After cocainization of the larynx, the bronchoscope was introduced A site in the right bronchus was selected for the obstruction The distance of this site from the upper teeth was carefully measured on the bron-

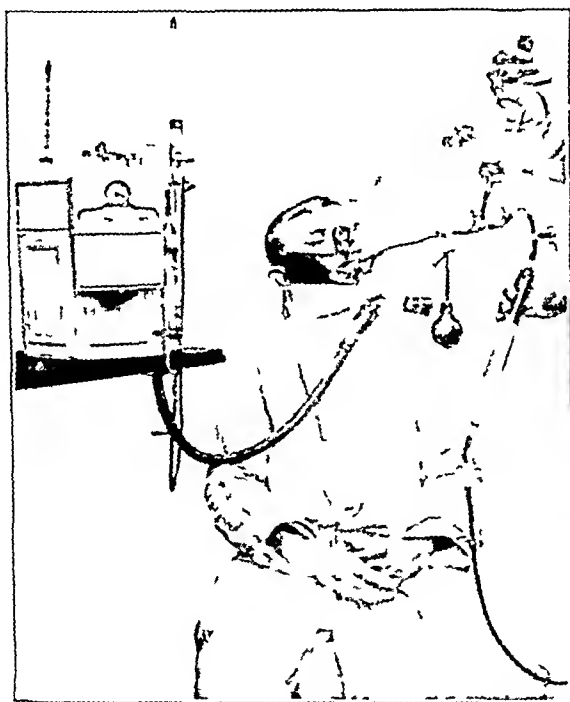


Fig 3—The Loewy and von Schroetter lung catheter introduced through the mouth and trachea into the right stem bronchus To the apparatus is connected a mouth valve which is connected to a spirometer (from Loewy and von Schroetter)

choscope, and the instrument was removed Then by the use of a tongue spatula, the patient being seated with the head in hyperextension the epiglottis was retracted, the glottis seen and the lung catheter gently introduced into the right bronchus so that the balloon was at exactly the distance previously recorded through the bronchoscope The balloon was then inflated and the mouthpiece if necessary put in place After a few trials the patient was accustomed to the apparatus so that Loewy and von Schroetter were able to maintain the apparatus in place for as long as forty-two minutes Specimens of gas were drawn every



minute or so from the oral end of the tube, so that it was possible to follow the successive modifications brought about in the composition of the entrapped alveolar air

The time necessary for the establishment of an equilibrium between the gases of the blood and alveolar air, according to Wolffberg, was short, only a few minutes for dogs. In the experiment on man by Loewy and von Schroetter, this was generally obtained within from six to seven minutes. Loewy and von Schroetter found that the size of the occluded part of the lung has little importance for the rapidity of establishment of the equilibrium. It even seems that when an entire



Fig 4—The same lung catheter (Loewy and von Schroetter) as in figure 3. The apparatus is introduced into the right stem bronchus through the tracheal fistula of a tracheotomized patient (from Loewy and von Schroetter)

lobe or an entire lung is occluded the equilibrium is established much more rapidly. This may have some bearing on the observations of Van Allen, Lindskog and Richter, that if a tertiary bronchus is obstructed air will penetrate the obstructed portion of the lung from the surrounding alveoli, through what they describe as "alveolar pores". We shall discuss this point later. Loewy and von Schroetter said, however, that the decrease in oxygen in the circulating blood following the occlusion of an important portion of the respiratory area, with unhampered circulation speeds up the passage of the alveolar oxygen into the capillary blood because of the increased differences in their

respective partial pressures. It is interesting to note here that Loewy and von Schroetter in this experimental work had already stated 1 Prolonged obstruction will necessarily lead to atelectasis by complete absorption of the alveolar air. 2 During this process of absorption the intra-alveolar pressure in the occluded lung remains within normal limits. They explained this fact in the following way. The arterial blood will be polluted by its mixture with unaerated blood coming from the obstructed lung, the percentage of carbon dioxide will rise and oxygen decrease proportionally to the area of the obstructed pulmonary segment. In order to expel the excess of carbon dioxide the healthy lung is proportionally hyperventilated. This is effected by deepening of the respirations much more than by the increase in respiratory rate. This increase in size of the healthy lung augments the effect of the elastic recoil of the obstructed alveoli in their process of collapse while the gases are being absorbed. This positive pressure, the value of which is regulated by the extent of the occluded pulmonary area, exactly neutralizes the "negative pull" which theoretically, at least, should be exerted on the shrinking alveoli of the obstructed lung. The data furnished by Loewy and von Schroetter were of great help to us although we discovered this article when our work was already terminated, we reached similar conclusions and used a somewhat similar technic completely independent of these authors.

It is peculiar that with the rather extensive clinical and pathologic knowledge concerning atelectasis, and notwithstanding these valuable data available in the literature none of the many investigators on atelectasis has put the mechanism of its production on a sound physiologic basis.

#### EXPERIMENTAL WORK

##### TECHNIC

In previous papers we showed that atelectasis can be constantly produced experimentally if a bronchus is obstructed in an air-tight manner. For this purpose we elaborated a specially constructed catheter with a one-way valve elastic balloon which was introduced by the bronchoscope in a chosen valve of the dog. This balloon described elsewhere, can be inflated from the outside and then detached from its connection and left in place. Roentgenographic examination of the animal placed on a special stand for obtaining symmetrical pictures shows the characteristic pictures of atelectasis with the displacement of the heart, the trachea and the diaphragm to the affected side, and opacity of the affected lung. We believe that if we were able to produce atelectasis regularly it was because we used as an obstructive agent an elastic balloon and not a solid plug of cork, wood or metal, such as that tried by others before and after our investigations. We are convinced that a solid body cannot com-

pletely obstruct a bronchus which yields and the diameter of which changes constantly with expiration and inspiration<sup>2</sup>

The solution of our present problem, however, required a new technic. We had to devise an instrument that would enable us to obstruct completely a bronchus through the bronchoscope—in order to avoid opening of the chest or trachea. We must also be able to draw alveolar air from below the obstruction for determination of gas percentages and intrapulmonary pressure. After a number of trials we constructed the following two types of apparatus, which gave us full satisfaction.

*Intrabronchial Cannulas*—The first apparatus is composed of two thin-walled brass tubes of 1 and 2 mm internal diameter, respectively, and 50 cm long. The external diameter of both tubes soldered together does not exceed from 6 to 7 mm, so that the instrument easily passes through Jackson's full lumen 9 mm bronchoscope. The narrow tube terminates 15 mm proximal to the larger one,

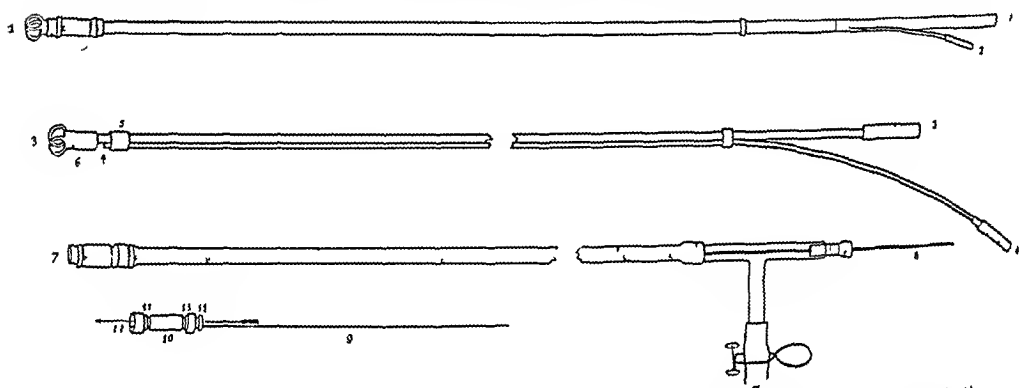


Fig 5—Intrabronchial catheters of Coryllos and Birnbaum. Model 1-1' is composed of a large external metal tube (5 mm in diameter) which terminates in a free end surrounded by a crown (1') in order to avoid closure of this end by bronchial mucosa. A smaller tube passes into this tube and emerges 15 mm from its distal end 1', where this tube is soldered, so that there is no connection between tubes 1 and 2. Around the distal end of the small tube is tied a piece of rubber tube, so that when air or fluid is introduced through 2 the rubber is distended, forming an obstructing balloon, as outlined. 3-3' is the model described in the text, showing 3-3' the larger, bronchial tube and 4-4' the smaller one which serves for the inflation of the obstructing balloon which is not depicted in the picture. 7-8 is the latest model, it is more detailed but is not essentially different from the preceding ones.

which is longer and has around its free end a wire crown to avoid obstruction by bronchial mucosa. For the same reason small lateral openings are made around this end. Above and below the distal opening of the small tube two brass rings are soldered around it, each of them bearing a groove for tying the small rubber balloon. Several models with more or less important modifications were made. In figure 5 1'-1 shows a bronchial catheter in which the small tube passes inside the larger tube throughout its length and emerges near its distal

<sup>2</sup> The ingenious tracheal cannula described by Van Allen and co-workers does produce a complete bronchial obstruction if well manipulated.

end, where it is filed down level with the outside tube, to which it is carefully soldered. Models 7 and 11 are the latest modification. A piece of fine india rubber tube (the tubing used for Kolman's urethral dilator is excellent) is put over the distal end of the cannula and securely tied around the groove with fine silk thread. This rubber tube is inflated through the small metal tube after the instrument is introduced into the chosen bronchus and forms an obstructing balloon. The accurate inflation of the balloon is one of the most important points of the technic. It must be sufficient to obstruct the bronchus completely, but not so excessive as to interfere with the circulation and innervation of the bronchus or with the ventilation of the other bronchus by displacement of the interbronchial spur or carina. These requirements are imperative, since as a rule these experi-

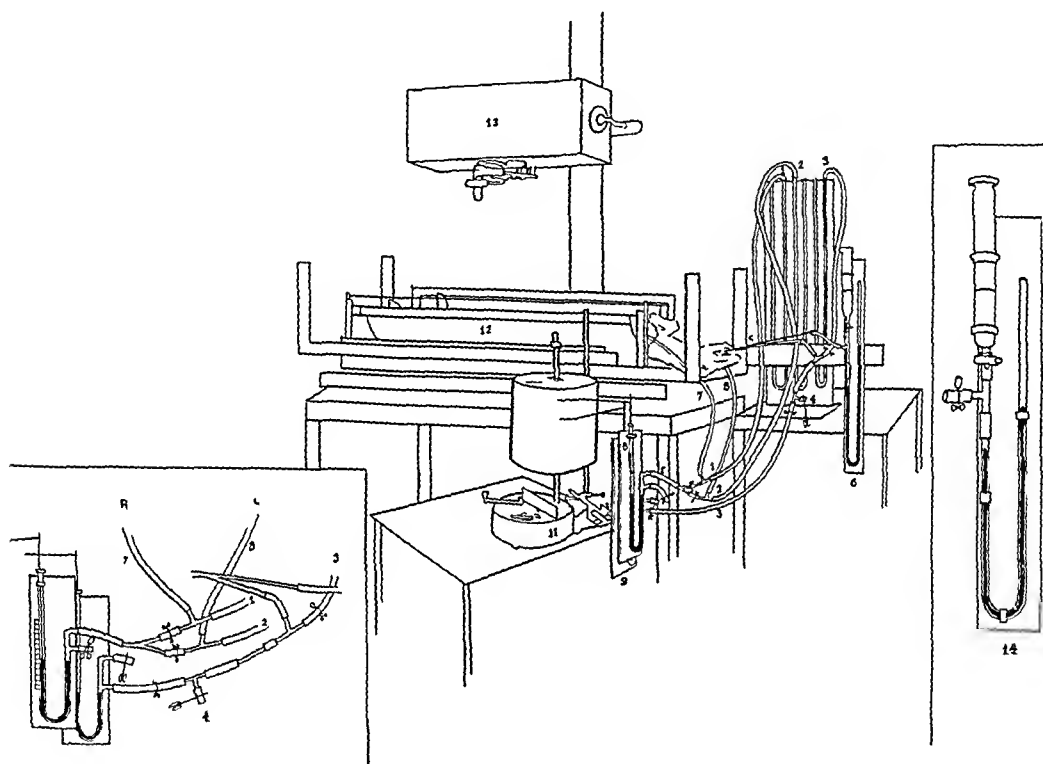


Fig 6—Lay-out of closed chest experiment. The animal is placed in our special X-ray stand (12) and the bronchus blocked by means of the intrabronchial catheter (5) connected to the mercury manometer 6, (enclosure 14) which allows checking up its degree of inflation. In each pleural cavity a cannula is placed connected to rubber tubes 7 and 8. These tubes are connected (left enclosure) by T tubes to water manometers (1 and 2) and through another tube to a recording mercury manometer, so that it is possible to record on the smoked drum the tracing of the right or left pleural cavity pressures. The large bronchial tube of the bronchial catheter is connected by a T tube to a water manometer (3) and to a mercury manometer recording on the same smoked drum (11). A T tube was interposed into the latter rubber tube (7 left enclosure) allowing the taking of air specimens of intrapulmonary air for gas analysis.

ments last for many hours. It is necessary to know at all times whether the degree of inflation and obstruction remains unchanged. For this reason we devised a closed mercury manometer system (fig 6, 14) the free end of which was connected by

way of a T tube to a syringe of 30 cc capacity. The horizontal tube was connected through a rubber tube to the small tube of the bronchial catheter. By pushing down the plunger of the syringe, already filled with water, we could inflate the balloon to a size a little greater than the estimated diameter of the bronchus on which bronchoscopy had previously been done, and a marker was placed at the height of the mercury meniscus in the closed end of the manometer. The bronchial catheter would then be disconnected. After it was introduced through the bronchoscope into the chosen bronchus, it would again be connected with the manometer and the plunger of the syringe pushed in to distend the balloon and bring the mercury meniscus slightly above the previously placed marker. As long as the mercury stood at this level we were certain that the balloon was inflated.

Two types of experiments were carried out.

*Closed Chest Experiment*—In the first group, which will be designated by 'closed chest experiment' (fig 6), the animal, under iso-amyl-ethyl barbituric anesthesia, was placed on the x-ray stand (12) so that the evolution of the experiment could be watched by fluoroscopy and roentgen-ray pictures. The intrapleural pressures during the experiment were taken by two water manometers (1, 2) connected with two cannulas introduced into the pleural cavities of the animal. Through the bronchoscope the pulmonary cannula was introduced and the balloon inflated, as already described. The larger tube of the bronchial catheter, which communicated with the entrapped pulmonary air, was connected to a water manometer (3), to a recording mercury manometer and at times through a T tube (4) to the sampling bulb for analysis of specimens of alveolar air. In this way it has been possible to follow simultaneously the intrapleural pressures and to record them on a smoked drum (11), to read and record the intrapulmonary pressure in the obstructed lung, to follow the changes in the percentage of the entrapped alveolar air and to check up by fluoroscopy and roentgenographic examination the progress of atelectasis. At the same time, the closed mercury manometer connected with the small tube of the intrabronchial catheter enables us to know exactly the degree of inflation of the obstructing balloon.

*Open Chest Experiment*—The second type of experiment will be designated "open chest experiment." In this series the chest of the animal (under iso-amyl-ethyl barbituric acid anesthesia) was opened by mediosternal section while intratracheal insufflation was being given. After careful hemostasis, the chest was widely retracted by two Balfour self-retaining retractors fixed to the edges of the wound by stitches passing through the intercostal spaces so as to avoid displacement. The animal was then carried to the oscillating vacuum box (fig 7), a detailed description of which has been given in a previous paper. The head was passed through the rubber tissue cuff (6, upper right angle enclosure) and this was applied around the previously shaved and petrolatum-anointed neck of the animal by means of cotton bandage (7). Intratracheal insufflation through the bronchoscope was only interrupted for the few seconds necessary to pass the head of the animal through the rubber cuff. Then the glass cover was applied and secured to the box to make it completely air-tight. In the meantime the rotating valve (8) was connected with the suction faucet (10) and the number of its revolutions per minute regulated to the respiratory rate of the animal as it was before opening of the chest. The intrapleural pressure was taken before operation and the oscillations of negative pressure in the box (indicated in the water manometer 9), were regulated so as to be equal to the intrapleural pressure of the

animal before opening of the chest. From now on the intratracheal insufflation must stop, and the animal will breathe with its chest wide open at the same rate and with the lungs under the same negative pressure as in the closed chest. Moisture and temperature inside of the box were kept as near normal as possible. Figure 8 is a photograph of the lay-out of the whole experiment. It has been repeatedly possible to keep the animal in fine condition in the box for from eight to fifteen hours. A small tube was provided for, through which saline solution could be given subcutaneously if necessary without disturbing the experiment.

We wish to point out that this box is based on a different principle from the differential pressure chamber of Sauerbruch. In the latter, only one pleural

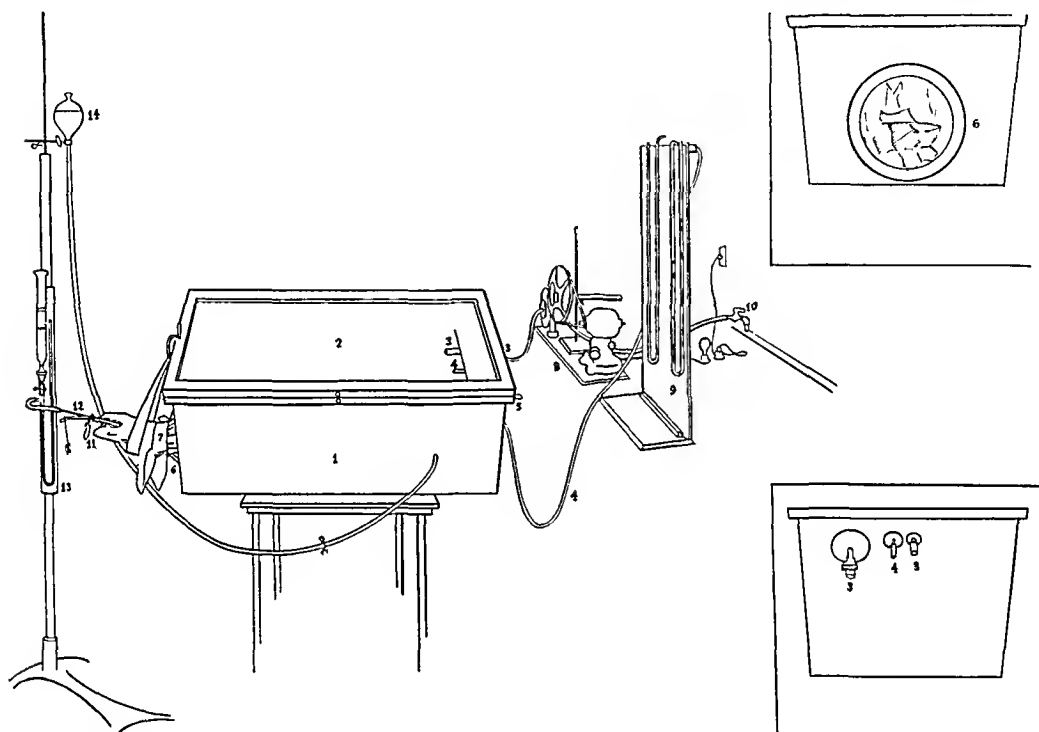


Fig 7—Lay-out of the open chest experiment in the oscillating vacuum box. After the chest is opened the animal is placed in the air-tight box (1) the cover of which (2) is made of plate glass. The head of the animal protrudes through the opening in the box, and the rubber tissue cuff attached around this opening (6, and upper left corner enclosure 6) is fixed around the neck of the animal, previously shaved and anointed with petrolatum, by a bandage (7). The rotating valve (8), interspersed between the suction apparatus (10) and the box inlet (3) insures an oscillating vacuum in the box. This pressure is measured by the water manometer (9) and is equal to the negative intrapleural pressure of the animal taken previous to operation. Inlet 5 serves to regulate the pressure in the box. A rubber tube passes through one wall of the box and is connected to a reservoir with physiologic solution of sodium chloride, by this means fluids can be administered under the skin or into the peritoneum of the animal during the experiment. Through the bronchoscope (11) the bronchial cannula is introduced into the left stem bronchus, and the balloon which is to occlude the bronchus is then inflated by means of the syringe-mercury manometer arrangement described in figure 6. The large tube of the cannula, in communication with the entrapped intrapulmonary air is closed off unless samples of air are to be withdrawn through it for gas analysis.

cavity being open, the steady and nonoscillating differential pressure (hypo or hyper) serves to keep the lung of the opened half-chest distended while the other lung breathes normally. In our box, on the contrary, both pleural cavities being widely opened, no respiration can take place unless there is an oscillation in the negative pressure box.

#### EXPERIMENTAL MATERIAL AND PURPOSE OF INVESTIGATION

The experiments were carried out exclusively on dogs, from 10 to 20 Kg in weight, because of the relatively large diameter of their tracheae and bronchi, which allow easy intrabronchial manipulation.

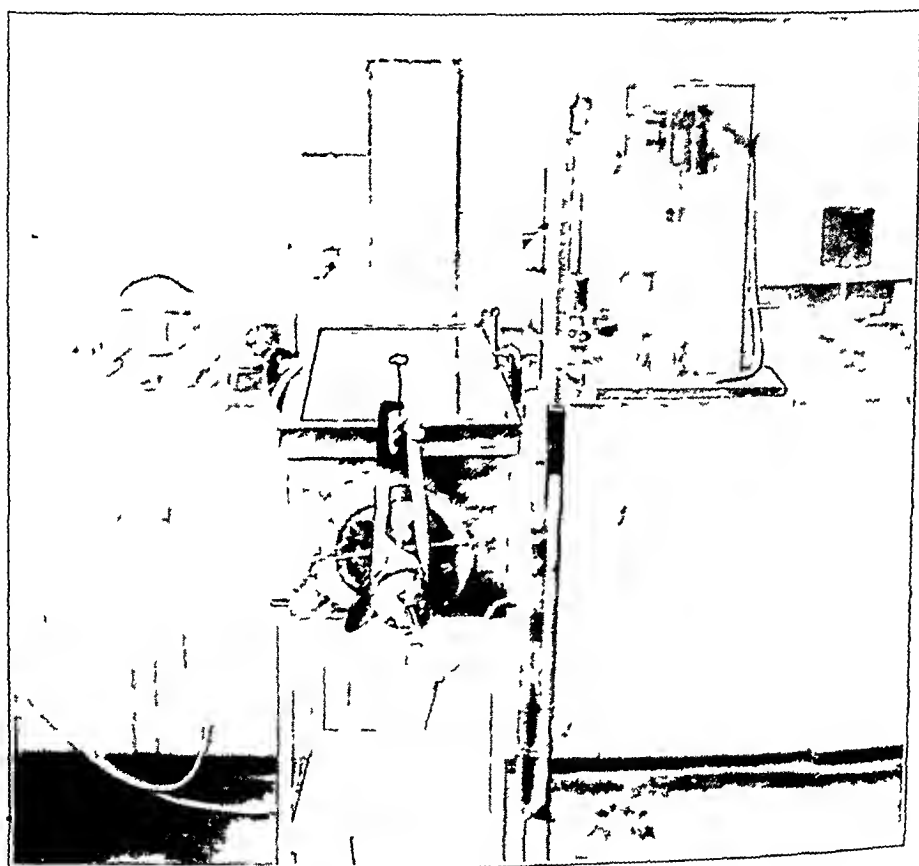


Fig 8—Open chest experiment series. Photographic view of the lay-out.

Forty-seven animals were used for this experimental investigation. They were anesthetized by the intraperitoneal injection of 10 per cent solution of iso-amyl-ethyl barbituric acid, 55 mg per kilogram of body weight being given with additional smaller doses after from five to six hours, thus prolonged anesthesia was made possible. Two animals died from the anesthetic. The others withstood the anesthetic well for the long duration of the experiment.

In this work the points investigated were the following:

- (1) The fate of the alveolar air entrapped in a pulmonary lobe after complete occlusion of the corresponding bronchus.

(2) The changes produced in the entrapped alveolar air as indicated by successive gas analyses

(3) Whether entrapped air is absorbed and at what rate

(4) The speed of absorption of the different gases composing the alveolar air (oxygen, carbon dioxide) when introduced individually into the lung of the living animal previously rendered atelectatic and what gas exchanges take place thereafter

(5) What happens when neutral gases are introduced separately into the atelectatic lung (nitrogen, hydrogen and helium)

(6) How the respiratory membrane behaves toward anesthetic gases or vapors (nitrous oxide ethylene, ethyl-chloride ether vapor)

(7) The changes, if any, in the intrapulmonary pressure during the process of gas absorption

The results obtained in successful experiments have been uniform, with small differences within limits of experimental error, inevitable with experiments so complicated and of such long duration. Before examining each of the foregoing questions separately the protocols of four experiments will be given two of the first type (closed chest) and two of the second type (open chest). Each of them is representative of the respective type.

#### ABSORPTION OF OXYGEN AND CARBON DIOXIDE

*Closed Chest Experiment* (dog 489) —The experiment lasted nine and a half hours

May 5 1930 11 45 p m The rubber balloon on the cannula was introduced into the right lower bronchus

11 52 p m The balloon was blown up with 3 cc of water

11 54 p m A sample of gas was obtained from the obstructed lung 15 cc it contained 5.85 per cent carbon dioxide and 9.05 per cent oxygen

12 03 p m A sample of gas contained 5.98 per cent carbon dioxide and 6.66 per cent oxygen

12 17 p m A sample of gas contained 5.9 per cent carbon dioxide and 6.43 per cent oxygen

12 28 p m A sample of gas contained 6.1 per cent carbon dioxide and 7.36 per cent oxygen

12 41 p m A sample of gas contained 6.07 per cent carbon dioxide and 6.15 per cent oxygen

12 52 p m A sample of gas contained 6.05 per cent carbon dioxide and 6.02 per cent oxygen

1 21 a m Only 2 cc of gas could be obtained

1 35 a m A roentgenogram showed a definite shift of the heart to the right

1 53 a m One hundred cubic centimeters of oxygen was introduced into the obstructed lung. Roentgenograms taken one and two minutes later showed the heart shifted to the left

1 58 a m A sample of gas from the obstructed lung contained 6.94 per cent carbon dioxide and 51.2 per cent oxygen

2 10 a m A roentgenogram showed the heart again back to the right side



- 2 15 a m Only 4 cc of gas could be obtained, this amount was insufficient for analysis
- 2 22 a m Fluoroscopy showed the heart a little more to the right than before the administration of oxygen The respiration was very quiet
- 3 50 a m Fluoroscopy showed increased density of the right lower lobe
- 5 26 a m One hundred cubic centimeters of carbon dioxide was introduced into the obstructed lung
- 5 26½ a m The heart was shifted to the left, the right lower lobe was clear
- 5 30 a m Only 48 cc of gas could be obtained It contained 54.16 per cent carbon dioxide
- 5 32 a m A roentgenogram showed the heart back again on the right, the breathing was very quiet
- 6 25 a m Fluoroscopy showed no further change, the right side of the diaphragm was immobile, and the heart moved toward the right on inspiration
- 9 15 a m A roentgenogram showed no change The animal was killed with 30 cc saturated solution of magnesium sulphate injected intravenously
- 9 20 a m Autopsy revealed atelectasis of the right lower and accessory lobes (confirmed by microscopic sections)
- Open Chest Experiment (dog 498)*—The experiment lasted fourteen hours, negative pressure was  $-4$ ,  $-7.5$  of water, oscillation rate, 14 per minute
- May 15, 1930 11 35 a m The left lung was obstructed
- 1 07 p m A sample of gas contained 60.9 per cent carbon dioxide and 47.4 per cent oxygen
- 8 30 p m Atelectasis was complete in nine hours
- 10 40 p m One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe
- 10 50 p m A sample of gas contained 8.59 per cent carbon dioxide, the oxygen percentage was beyond the limit of the apparatus
- 11 00 p m The left lower lobe was again atelectatic, all the gas was absorbed
- 11 10 p m One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe
- 11 20 p m The left lower lobe was again atelectatic, all gas was absorbed
- 11 25 p m One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe
- 11 31 p m The left lower lobe was much smaller, 100 cc more of oxygen was introduced
- 11 35 p m A sample of gas contained 10.63 per cent carbon dioxide, the oxygen percentage was beyond the limit of the apparatus
- 12 13 a m One hundred cubic centimeters of carbon dioxide was introduced to distend the left lower lobe
- 12 14½ a m All the carbon dioxide was absorbed, the lobe was again atelectatic
- 12 16 a m One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe again
- 12 27 a m The oxygen was completely absorbed the lower left lobe was again atelectatic
- 12 37 a m Fifty cubic centimeters of oxygen and 50 cc of carbon dioxide was introduced to distend the lower left lobe

12 38 a m A sample of gas contained 30 per cent of carbon dioxide, the sample was insufficient for oxygen analysis

12 41 a m All the gas was absorbed, the lobe was again atelectatic

1 02 a m One hundred and fifty cubic centimeters of 100 per cent ether vapor was introduced to distend the lower lobe

1 03 a m All the ether was absorbed, the lobe was atelectatic again

1 09 a m One hundred cubic centimeters of nitrogen was introduced into the left lower lobe

1 25 a m The heart stopped beating, the lung was unchanged

Summary The absorption time for oxygen averaged 15 minutes, for carbon dioxide, 15 minutes, for equal parts of carbon dioxide and oxygen, 4 minutes, for 100 per cent ether vapor, 1 minute

#### ABSORPTION OF VARIOUS GASES BY THE LUNG

*Closed Chest Experiment* (dog 511) —The dog weighed 22 Kg Fluoroscopic and roentgenographic control was employed

May 23, 1930 2 00 p m Iso-amyl-ethyl barbituric acid, 60 mg per kilogram of body weight, was used The animal was asleep at 2 14 p m

3 45 p m The animal was placed on the stand, a double bronchial cannula was introduced, and the left lung obstructed by inflation of the balloon

4 30 p m The left lung was irrigated with oxygen It appears that the side of the cannula was obstructing the left upper lobe and the balloon the left lower lobe, but the obstruction did not seem complete because on aspiration of the cannula the lung did not appear to decrease in size under fluoroscopy

5 30 p m The left lung was again blocked and irrigated seven times with oxygen

5 35 p m In the first roentgenogram the oxygen was shown to be absorbing

6 30 p m A second roentgenogram was taken

7 05 p m Oxygen 275 cc, was introduced into the left lung by means of the pneumothorax apparatus which registered an intrabronchial pressure of from + 1 to 2 during the introduction A third roentgenogram was made (fig 9 A)

7 20 p m A fourth roentgenogram showed complete absorption of oxygen in the left lower lobe (fig 9 B)

7 35 p m No further change was noted, 225 cc of oxygen was again introduced A roentgenogram was made

7 52 p m Fluoroscopy showed complete absorption of gas

8 00 p m Carbon dioxide, 290 cc, was introduced (fig 10 A)

8 05 p m Fluoroscopy showed complete absorption of gas

8 10 p m A roentgenogram confirmed the fluoroscopic observation

8 30 p m Fluoroscopy showed perhaps a slightly greater absorption than at 8 10

8 47 p m Nitrous oxide, 280 cc, was introduced into the left lower lobe (fig 11 A)

8 58 p m The roentgenogram showed practically complete absorption of the gas (fig 11 B) With a syringe 5 cc of serous fluid and 2 cc of frothy material was aspirated from the left lower lobe This is the first time fluid has been noticed

9 05 p m Seven cubic centimeters of slightly frothy fluid was aspirated from the left lower lobe

9 10 p m One cubic centimeter of fluid was aspirated Fluoroscopy showed no further absorption of nitrous oxide

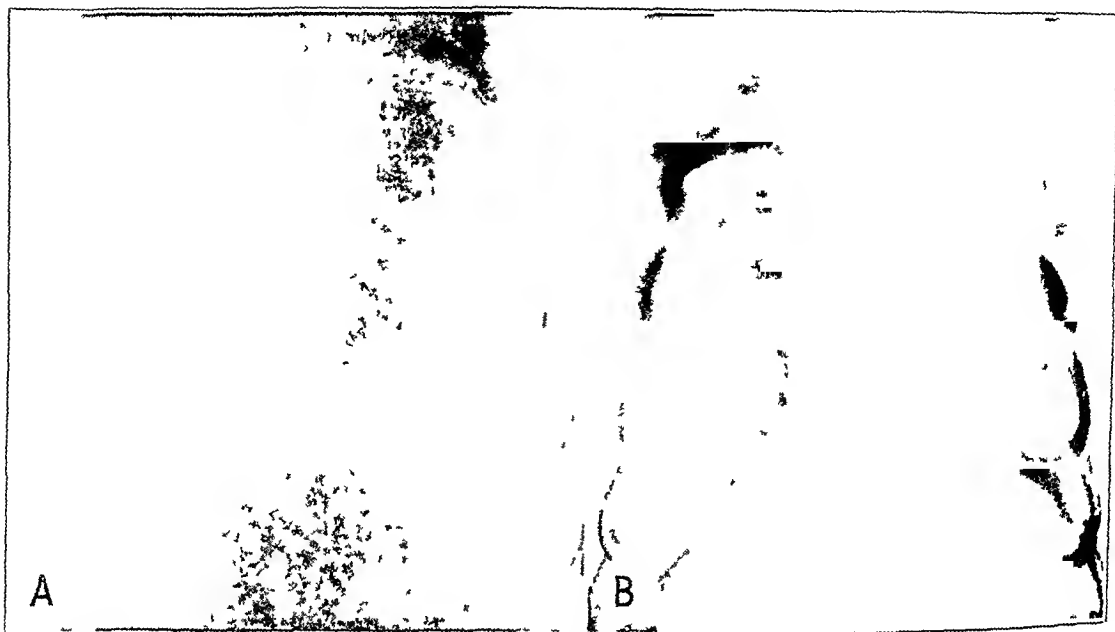


Fig 9 (dog 511) —*A* was taken after the introduction of 275 cc into the left lower lobe which appears distended, *B*, fifteen minutes after the introduction of 275 cc of oxygen into the lower left lobe. The gas has been completely absorbed. The clear area at the base of the left lung is due to an abnormal position of the accessory (right) lobe, as proved by autopsy. See figure 15.

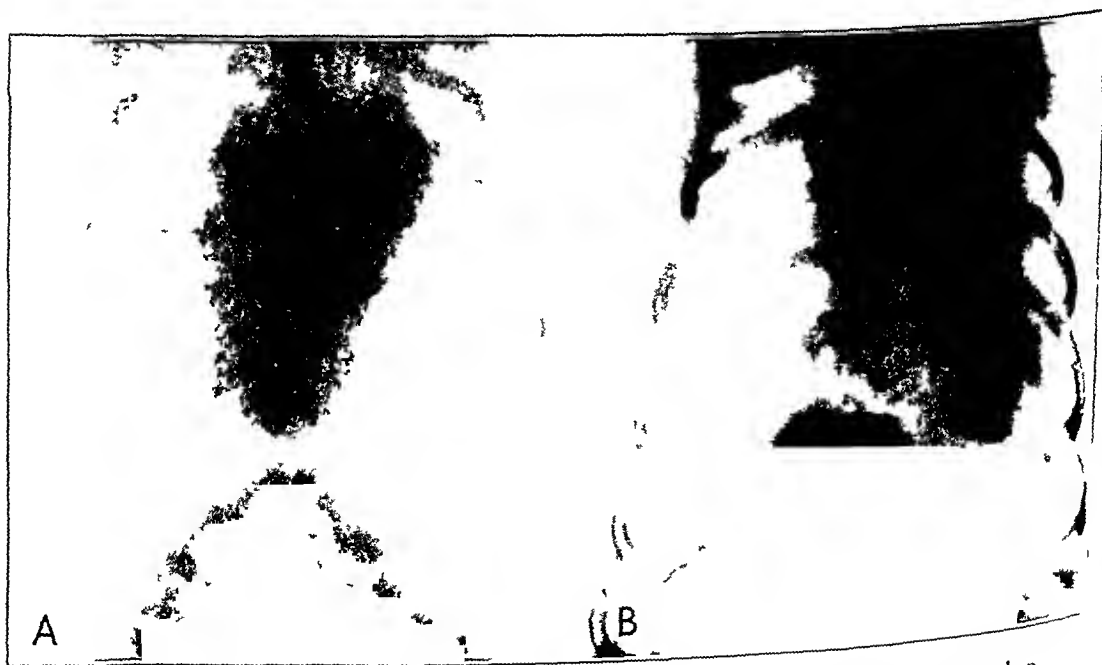


Fig 10 (dog 511) —*A* was taken after the introduction of 250 cc of carbon dioxide into the left lower lobe which appears distended. *B*, ten minutes after the introduction of carbon dioxide into the left lower lobe. The gas has been completely absorbed.

9 25 p m Roentgenogram showed that nitrous oxide had been absorbed. Three cubic centimeters of frothy fluid was extracted from the left lower lobe.

9 40 p m Oxygen 275 cc. was introduced into the left lower lobe and a roentgenogram made.

9 55 Oxygen was absorbed, as shown by fluoroscopy.

10 10 p m Two hundred and fifty cubic centimeters of ethylene was introduced (fig. 12 F).

10 22 p m Fluoroscopy showed practically complete absorption.

11 35 p m Seven cubic centimeters of free gas and 24 cc. of serous fluid were extracted from the left lung by a syringe. A roentgenogram showed no further change (fig. 12 B).

May 24 12 30 i m Three and a half cubic centimeters of iso-amyl-ethyl barbituric acid was given peritoneally. Fluoroscopy showed no further change.

6 30 i m One and one half cubic centimeters of mucoserous fluid was removed from the left lung and a roentgenogram made.

7 10 i m Oxygen 280 cc. was introduced into the left lung.

7 20 i m About 2 cc. of free gas could be withdrawn through the bronchial cannula from the left lower lobe.

7 24 i m Fluoroscopy showed the absorption of oxygen to be complete.

7 25 i m Carbon dioxide 275 cc. was introduced into the left lung.

7 30 i m The absorption of carbon dioxide was complete, no serum.

7 35 i m Ethylene 275 cc. was introduced into the left lung.

7 47 i m Seventeen cubic centimeters only of free gas could be withdrawn with a syringe from the left lower lobe, which was again injected in the lung.

8 20 i m Fifteen cubic centimeters of free gas could be withdrawn from the left lung; this gas was returned to the lung, as in former instances. No fluid could be withdrawn. A roentgenogram was made. This was no different than ten minutes after introduction of ethylene. The great mass of the gas was absorbed rapidly, the rest taking a long time.

9 15 a m There was still 15 cc. of free gas that could be withdrawn from the left lower lobe. 12 cc. was returned to the lung. The gas in the syringe smelled like ethylene.

9 40 i m Twelve cubic centimeters of gas could still be withdrawn easily.

10 00 a m Ten cubic centimeters of gas could still be withdrawn easily; this was not returned to the lung. Four cubic centimeters of iso-amyl-ethyl barbituric acid was given peritoneally.

1 40 p m Oxygen, 275 cc., was introduced into the left lower lobe.

1 52 p m The absorption of oxygen was complete, as seen by fluoroscopy; no fluid could be aspirated.

1 54 p m Carbon dioxide, 250 cc., was introduced into the left lower lobe.

1 57 p m Absorption seemed complete by fluoroscopy; no fluid could be withdrawn.

2 08 p m Nitrous oxide (water washed), 250 cc., was introduced into the left lung.

2 12 p m Only thirteen cubic centimeters of free gas could be withdrawn; it was returned to the lung.

2 15 p m Eleven cubic centimeters of free gas could be withdrawn; it was returned to the lung.

2 20 p m Ten cubic centimeters of free gas could be withdrawn; this 10 cc. was rejected; there was no serum or fluid.

2 25 p m No fluid or mucus could be withdrawn.

2 26 p m Nitrous oxide (dry), 250 cc., was introduced into the left lung.



Fig 11 (dog 511) —*A* was taken after the introduction of 280 cc of nitrous oxide into the left lower lobe, *B*, eleven minutes after the introduction of 280 cc of nitrous oxide. The gas has been absorbed.

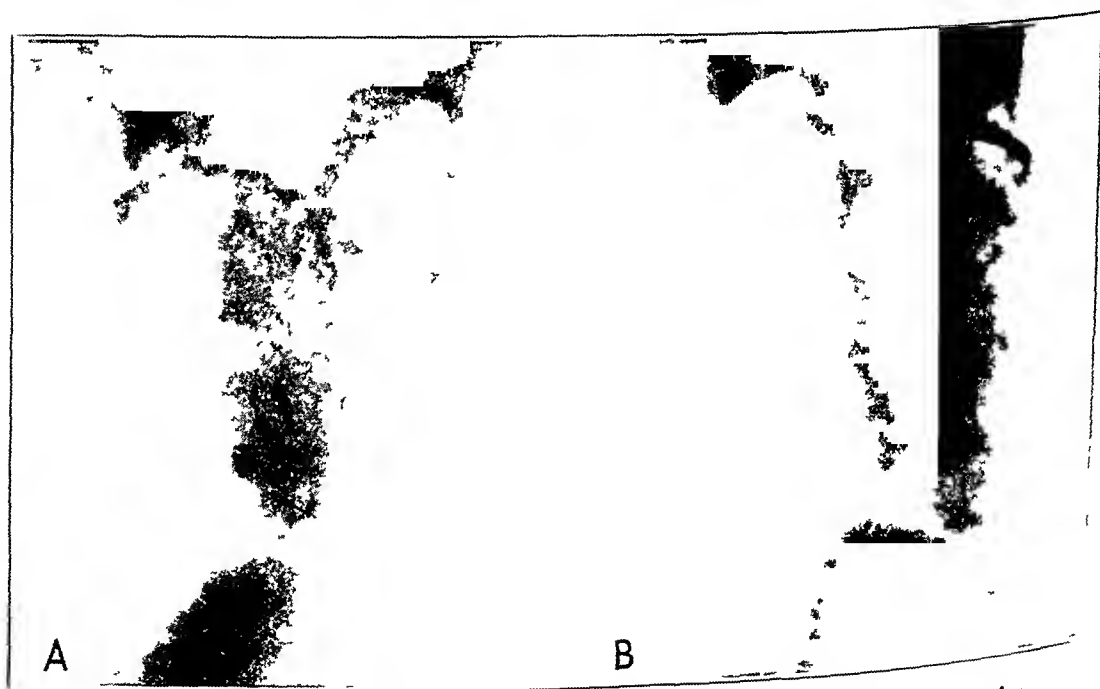


Fig 12 (dog 511) —*A* was taken after the introduction of 250 cc of ethylene into the left lower lobe, *B*, after the absorption of ethylene.

- 2 30 p m Fourteen cubic centimeters of free gas could be withdrawn, it was returned to the lung
- 2 33 p m Eleven cubic centimeters of free gas could be withdrawn, it was returned to the lung
- 2 39 p m Nine and one-half cubic centimeters of free gas could be withdrawn, it was returned to the lung
- 2 48 p m Nine cubic centimeters of free gas was withdrawn from the lung and rejected, no fluid or mucus was found
- 2 52 p m The left lung was irrigated three times with oxygen
- 2 57 p m Absorption seemed complete by fluoroscopy, no fluid could be withdrawn
- 3 17 p m Nitrous oxide, 20 cc, was introduced into the left lower lobe
- 3 18 p m Twelve cubic centimeters of free gas could be withdrawn, it was returned to the lung
- 3 19 p m Seven cubic centimeters of free gas could be withdrawn, it was returned to the lung
- 3 20 p m Four cubic centimeters of free gas could be withdrawn, it was returned to the lung
- 3 22 p m Three cubic centimeters of free gas could be withdrawn, it was returned to the lung
- 5 50 p m The absorption of gas seemed complete by fluoroscopy. A mixture of equal parts of helium and oxygen, 200 cc, was introduced into the left lower lobe, and a roentgenogram made
- 7 20 p m A roentgenogram showed partial absorption of gas
- 8 00 p m Analysis of the gas showed 5.86 per cent oxygen and 8.29 per cent carbon dioxide. The remainder of the free gas in the lung, 116 cc, was aspirated. No fluid or mucus was found. Fluoroscopy showed the lung to be collapsed
- 8 08 p m One-half cubic centimeter of mucus was aspirated
- 8 10 p m A roentgenogram was made
- 8 30 p m The left lower lobe was irrigated three times with helium and then 175 cc of helium (pure water-washed) was introduced into the left lower lung. Fluoroscopy showed the lower lobe to be distended
- 9 15 p m By fluoroscopy, the left lower lobe seemed slightly increased in size
- 9 20 p m Twenty cubic centimeters of gas was withdrawn from the lung for analysis, which showed 5.83 per cent oxygen and 9.34 per cent carbon dioxide
- 10 30 p m There was no apparent change in the lung
- 12 00 p m There was no apparent change in the lung
- May 25, 1 00 a m Thirty-five cubic centimeters of gas was withdrawn from lung for analysis, which showed 5.34 per cent oxygen and 6.22 per cent carbon dioxide
- 1 10 a m One hundred and forty cubic centimeters of gas was withdrawn leaving 15 cc of available gas in the lung. Fluoroscopy showed the left lower lobe almost totally collapsed
- 2 00 a m The last 18 cc of available gas was withdrawn for analysis, which showed 5.25 per cent oxygen and 6.64 per cent carbon dioxide
- 2 10 a m The lung was irrigated five times with oxygen
- 2 15 a m No free gas or fluid could be aspirated. Fluoroscopy showed complete collapse
- 2 20 a m Two and one-half cubic centimeters of iso-amyl-ethyl barbituric acid was administered

3 30 a m Eighty cubic centimeters of physiologic solution of sodium chloride was given subcutaneously

9 10 a m Fourteen and one-half cubic centimeters of iso-amyl-ethyl barbituric acid was given The dog breathed quietly

11 00 a m A roentgenogram was made

12 25 p m A roentgenogram was made

12 30 p m The animal was killed by intravenous injection of 10 cc of a saturated solution of magnesium sulphate

Post Mortem The left upper lobe was completely atelectatic The left lower lobe was completely atelectatic and moderately edematous (hg 13)

*Open Chest Experiment* (dog 504) —The dog weighed 12 Kg

May 17, 1930, 10 30 a m Iso-amyl ethyl barbituric acid 60 mg per kilogram of body weight, was given



Fig 13 (dog 511) —Posterior view of the (left, atelectatic) lung extracted from the chest

11 55 a m Ephedrine sulphate one-half gram (0.32 mg) was given subcutaneously the respiratory rate was 16, the pulse rate 140

12 00 a m The animal was placed in the vacuum box, the respiratory rate was 12, the pulse rate 145

12 37 p m The left lung was obstructed, had been washed out six times with oxygen and left inflated with oxygen

1 40 p m Atelectasis was progressing slowly The lung was re-washed once with oxygen

1 52 p m The bronchial cannula was withdrawn

1 58 p m The cannula was reintroduced and the balloon inflated

2 00 p m The whole left lung was aspirated seven times and oxygen introduced each time The lung was then aspirated and left in the collapsed state

2 15 p m The respiratory rate was 10, the pulse rate 128. The manometer excursion (one-half the actual value) was  $-2$  to  $-7$  cm of water.

2 33 p m A long glass tube was connected to the bronchial catheter and allowed to dip down into a large beaker of water which was placed 2 feet (60.91 cm) below the level of the catheter. It was noticed that on inspiration water was sucked up to a height of 8 cm and on expiration the height of the column went down to 6 cm.

2 50 p m Nitrous oxide was introduced from a tank into a large leveling bulb, immersed under water to wash out the air and fill it with the gas. It was then disconnected from the tank and its outlet connected to the obstructed lung. In this way 175 cc of the gas was introduced over a period of four minutes.

3 05 p m The respiratory rate was 12, the pulse rate 168 (spontaneous respiration five per minute).

3 17 p m There were rapid respiratory movements independent of the manometer excursion. Two cubic centimeters more of iso-amyl-ethyl barbituric acid one-fourth grain (16 mg) of morphine and 2 mg of atropine was given subcutaneously.

3 25 p m The lower lobe was almost entirely blue, the upper lobe was slightly so. The temperature was  $40^{\circ}\text{C}$  ( $104^{\circ}\text{F}$ ).

3 30 p m The lower lobe was atelectatic. The upper lobe was further advanced but not completely useless.

3 35 p m The lower lobe was completely atelectatic.

3 36 p m The temperature in the box was  $34^{\circ}\text{C}$ .

3 38 p m The upper lobe was completely atelectatic except for a small portion at the hilus and a small part of the periphery.

3 45 p m Carbon dioxide (175 cc) was introduced into the left lung to distend it to the same size it was with nitrous oxide (175 cc).

3 47 p m The gas was absorbing rapidly.

3 53 p m There was a diffuse patchy involvement over the entire surface of both left lobes.

4 02 p m Atelectasis was complete in both lobes of the left lung.

4 04 p m Ethyl chloride vapor was introduced directly into the left lung, introduction was complete at 4 04½.

4 06 p m Atelectasis progressed rapidly.

4 10 p m The pulse rate was 172, the respiratory rate 12, the spontaneous respiratory movement was 56.

4 14 p m Atelectasis was complete.

4 16 p m Ethylene (175 cc) was introduced directly into the left lung.

4 27 p m Absorption was going on slowly, reflexes were present.

4 45 p m Atelectasis was complete in the lower lobe except at the periphery. In the upper lobe, atelectasis was beginning in the midportion of the lung.

4 48 p m Both lobes were about the same as before, the pulse rate was 180, respiratory rate 12 and spontaneous respiration 56 and irregular. The manometer excursion was  $-2$  to  $-7$  on one half of the manometer limb.

5 15 p m Atelectasis was still progressing slowly. The tip of the upper lobe and the periphery were still expanded.

5 21 p m Atelectasis was progressing definitely but slowly, reflexes were present.

5 29 p m Atelectasis was complete.

5 31 p m Carbon dioxide (200 cc) was introduced into the left lung over a period of forty-five seconds to distend it completely. The tip of the upper portion of the upper lobe had become dry and adherent to the mediastinum.



- 5 35 p m Absorption was going on rapidly
- 5 43 p m Atelectasis was complete in the lower lobe It had progressed further in the lower part of the upper lobe than in the upper part of the upper lobe
- 5 52 p m Atelectasis was complete
- 5 53 p m Ethyl chloride (500 cc) was again introduced into the left lung over a period of two minutes It appeared that absorption was going on as fast as the gas was introduced It was difficult to inflate the lung
- 5 55 p m The animal was deeply cyanotic, the pulse rate was 180, the pupils were dilated, and the reflexes were absent
- 5 59 p m Absorption progressed rapidly
- 6 05 p m The eye reflex had returned, cyanosis had disappeared
- 6 10 p m The rate of absorption was definitely slower The lower lobe was practically completely atelectatic The upper lobe, especially the upper portion, was still slightly expanded
- 6 15 p m The pulse rate was 168, the manometric respiration, 14, spontaneous respiration, 48 The manometer excursion was  $-35$  to  $-85$  cm of water
- 6 30 p m Atelectasis was complete except in portions of the upper part of the upper lobe
- 6 39 p m Atelectasis was complete except at the periphery of the upper part of the upper lobe
- 6 45 p m Atelectasis was complete
- 6 48 p m Carbon dioxide (300 cc) again was introduced over a period of thirty seconds
- 6 59 p m Absorption thus far had been fairly rapid There was no definite area of atelectasis yet visible
- 7 05 p m Absorption was progressing somewhat slower
- 7 15 p m The lower lobe and a large portion of the lower part of the upper lobe were atelectatic
- 7 20 p m The pulse rate was 168, manometric respiration, 18, spontaneous respiration, 18 The manometric excursion was  $-25$  to  $-7$  cm of water
- 7 30 p m Atelectasis was complete in the lower lobe The upper lobe and tip of the lower half were expanded, especially at the periphery
- 8 00 p m Atelectasis was complete except for a strip at the center and the periphery of the upper portion of the upper lobe
- 8 10 p m Atelectasis was complete The pulse rate was 176, manometric respiration, 18, spontaneous respiration, 20 Manometric oscillation was from  $-3$  to  $-7$  cm of water
- 8 12 p m Ethylene (300 cc) was introduced into the lung over a period of two minutes The last portion of the lung to collapse was the first to expand
- 8 25 p m The lower lobe and lower portion of the upper lobe was almost completely atelectatic The upper portion of the upper lobe showed patchy atelectasis
- 8 40 p m Atelectasis was complete except for a strip in the center of the upper lobe and scattered portions of the periphery of the upper lobe
- 8 45 p m Atelectasis was complete
- 8 46 p m Oxygen (300 cc) was introduced into the left lung to expand it to previous size
- 8 48-8 55 p m The motor on the suction machine stopped It was necessary to rotate the valve by hand till the motor was adjusted
- 9 00 p m Absorption of oxygen had progressed rapidly Atelectasis was nearly complete except for the periphery of the upper part of the upper lobe

9 04 p. m. The pulse rate was 164 both the manometric and spontaneous respirations were 18. The manometric excursion was  $-1$  to  $-8.5$  cm. of water.

9 05 p. m. Atelectasis was complete except for a few areas at the periphery of the upper part of the upper lobe.

9 07 p. m. Atelectasis was complete.

9 13 p. m. Ether vapor was introduced over a period of one minute and a half.

9 16 p. m. The left lung collapsed but remained pink in color—not the liver-like appearance of atelectasis.

9 22 p. m. Atelectatic areas were appearing in the lower lobe and lower portion of the upper lobe. Absorption was going on at a moderate rate. The animal was showing extreme cyanosis.

9 23 p. m. The heart was very irregular.

9 25 p. m. The animal died.

Post Mortem. The left upper lobe was completely atelectatic, the left lower lobe was edematous, friable and hemorrhagic.

Figures 14 *A* and *B* are histologic sections of the upper lobes in closed and open chest experiments showing complete atelectasis. Figure 15 showed interstitial hemorrhage and edema of the lung produced by the introduction of ether vapor into a lung previously rendered atelectatic.

#### PROBLEMS INVESTIGATED

I *Fate of Alveolar Air Entrapped in a Pulmonary Lobe After Complete Occlusion of Corresponding Bronchus*.—In all our experimental animals atelectasis was produced within from six to fifteen hours. They were all under deep anesthesia so that the point raised by Van Allen and Adams, namely, that animals with a lobar or larger bronchus obstructed do not get atelectasis unless they are insufficiently anesthetized or have strained respiration, is not verified by our experiments. On the other hand, we believe that the assertion of these authors that when a tertiary lobe is occluded atelectasis does not occur is correct but we do not agree entirely as to the explanation of this phenomenon given by them. They attribute it to the passage of air from the adjoining alveoli through microscopic holes—the alveolar pores present in the interalveolar spaces. Such pores do really exist and were described long ago. A. Nicolas, in Poncet's textbook of anatomy (vol. 4, p. 528) said, "Is the homogeneous hyaline membrane, which with the respiratory epithelium constitutes the wall of the alveoli, normally perforated or not?" It is generally conceded that in aged persons interalveolar perforations can be observed due to local resorption and atrophy of the respiratory membranes. The majority of authors (Shultz, Koelliker, Water, F. E. Shultze) deny the existence of these alveolar pores in normal persons. Others (Hauseman, F. Meikel) just as affirmatively argue their existence." Letulle (vol. 1, p. 13) does not admit their existence in normal lungs of young persons but believes they may exist in advanced age and calls them "trous d'usure." This

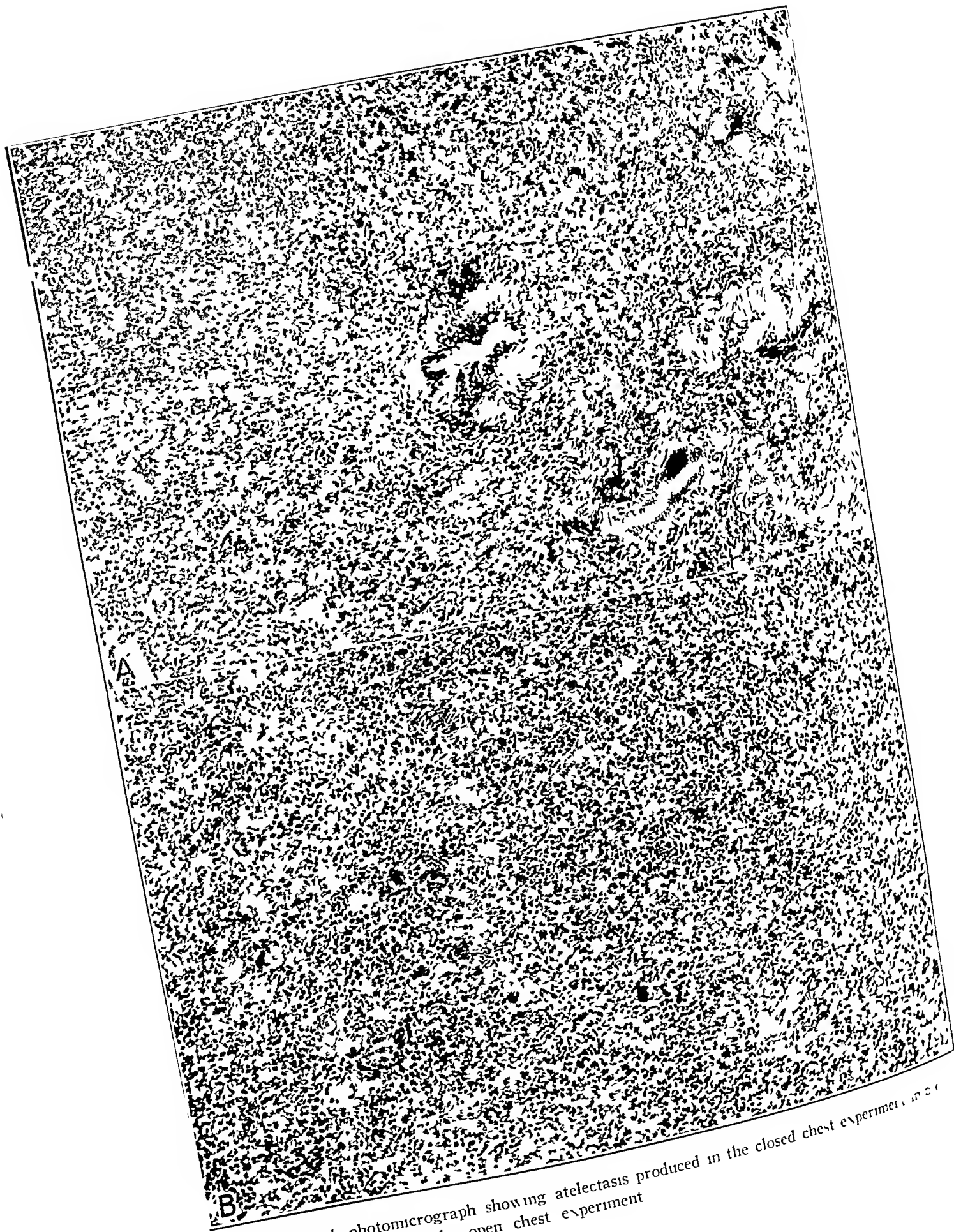


Fig 14—1 photomicrograph showing atelectasis produced in the closed chest experiment  
B, atelectasis produced in the open chest experiment

discussion brings to mind the discussion about the existence of similar pores in the mediastinum of the dog. This latter problem is solved today in favor of the nonexistence of anatomic pores permitting direct communication between the two pleural cavities, but the mediastinum of the dog is none the less readily permeable to air and even to fluids. The same reasoning applies to the extremely thin respiratory alveolar endothelium and there is no necessity for real anatomic openings to explain the ready diffusion of air through the interalveolar septums. A definite experimental proof of this conception lies in the fact that

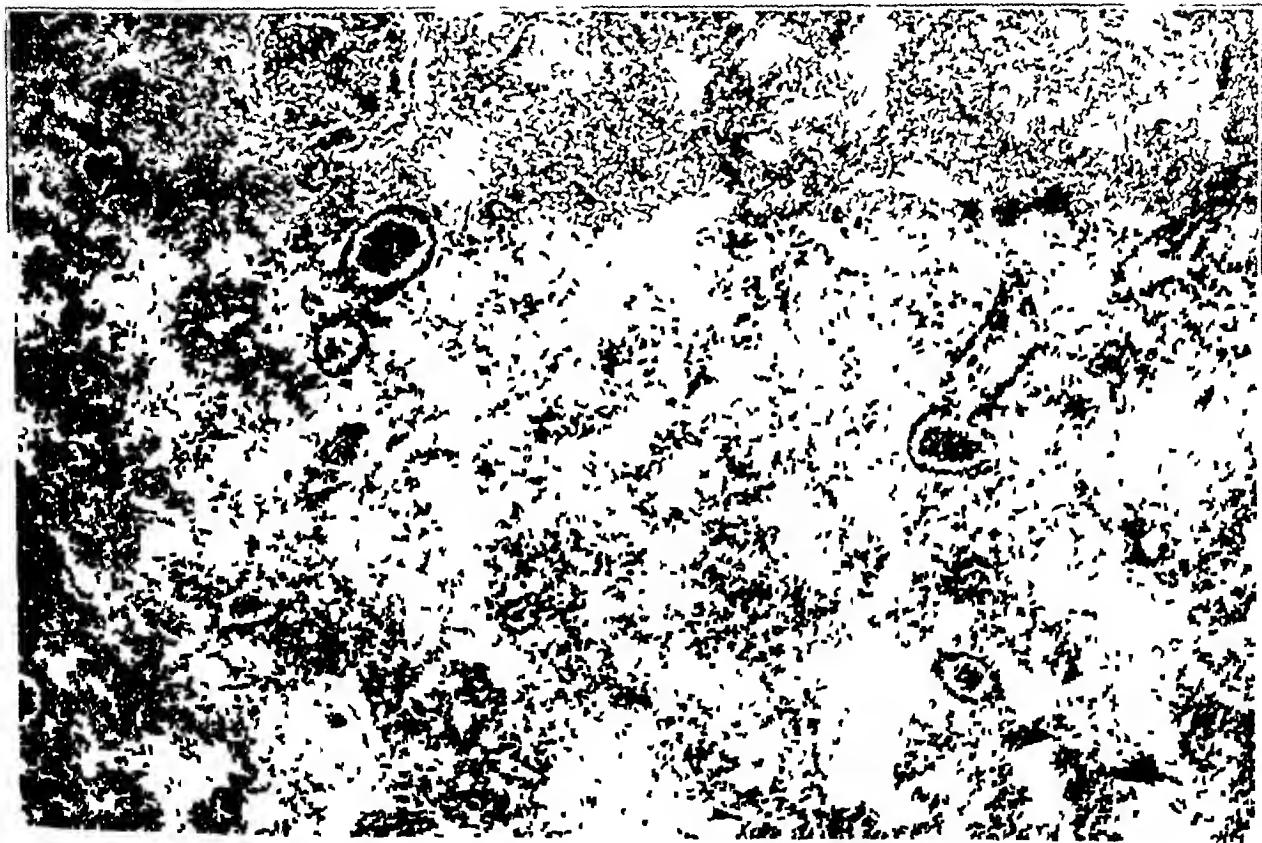


Fig. 15—Interstitial hemorrhage and edema in the left lower lobe after introduction of 100 per cent ether vapor into the lung previously rendered atelectatic (open chest experiment)

whereas air comes out freely through the cannula obstructing a tertiary bronchus and continues to come out for hours, it will stop immediately if we introduce through the cannula a few cubic centimeters of 100 per cent ether vapor, which produces edema of the alveolar epithelium. This may show that patchy atelectasis cannot occur in a healthy lung, but just as soon as there is a slight inflammatory edema it is produced exactly in the same way as when a lobal bronchus is occluded. So much for bronchiolar obstruction.

Such a controversy does not exist when a lobal or common bronchus is obstructed. Atelectasis may require more or less time to be completed but it inevitably occurs provided the lung circulation is normal and the alveolar endothelium not greatly altered. Increase in intrapulmonary pressure or a temporary one-way valve obstruction allowing air to be expired but not inspired naturally does accelerate the completion of atelectasis. In the case of increased intrapulmonary pressure, this acceleration would occur because of increase in the total and consequently of the partial pressures of the alveolar gaseous components (see comment), in the second case it would occur, if such a mechanism is really possible in man, with the anatomic funnel-like configuration of the bronchial tree because a portion of the alveolar air is mechanically eliminated, thus leaving less air to be absorbed. This is exactly what happened in the dogs of Van Allen and Adams when a portion of the air was allowed to be eliminated from the occluded lung. But in every case, when a big bronchus is occluded, atelectasis will follow. This statement is proved in our own case by many experiments on dogs (over 400), with roentgenographic and postmortem control. Moreover, in the experiments with the open chest it is easy to follow up the production of atelectasis by direct vision and to produce it at will and at different speeds by varying quantitatively and qualitatively the composition of the alveolar gaseous content. If atelectasis is not produced after bronchial obstruction, this means that the obstruction is not complete. Of the completeness of the obstruction, there is but one real proof. This is the rapid decrease in the percentage of oxygen in the alveolar air. We think we may state that when within ten minutes after bronchial obstruction the oxygen in the alveolar air does not decrease from 15 or 16 per cent to about 6 per cent, there is not complete bronchial occlusion. This principle, if used as a criterion in every experimental work on atelectasis, will avoid the making of many unwarranted statements. Such being the case, apneumatoses (airlessness) always following complete bronchial obstruction, there is but one other way for the air to leave the lung, the venous alveolar blood. A positive proof of this will be given.

In the compressed lung as in open or tension pneumothorax or when fluid is present in the pleural cavity, the mechanism of atelectasis contrary to the prevailing opinion, is exactly the same. In fact when the lung collapses the small bronchioles collapse at the same time and their lumen is obstructed. Proof of this is that air is entrapped in the alveoli which will remain there, unless life, and with it, circulation continue for a sufficient length of time. Lichtheim proved this fact in 1879. Collapsed lung is not synonymous with atelectatic or apneumatic (airless) lung the difference between them being that alveolar air is present

in the former. How then would this air remain in the perfectly elastic alveoli if there were no bronchial obstruction due to the collapse of the bronchiole and ducti alveolares and how would this air disappear after a while unless it were absorbed by the circulatory blood? Therefore we believe that there is no difference whatever in the production of atelectasis in the obstructed and in the compressed lung.

II *Changes Produced in Entrapped Alveolar Air as Indicated by Successive Gas Analyses*—The results obtained in closed as well as in open chest experiments show that within from two to seven minutes after bronchial obstruction the oxygen and carbon dioxide percentages fall rapidly to from 5 to 6 per cent, as seen in the tables they remain at about the same figures until the complete disappearance of the alveolar air. Our results absolutely corroborate the results obtained under

TABLE 3—*Changes in Oxygen and Carbon Dioxide Percentages After Obstruction*

Dog	Time After Obstruction	Oxygen	Carbon Dioxide	Comment
466	Before bronchial obstruction	14.20	4.80	
	5 minutes		4.09	
	15 minutes	2.09	4.12	Animal dyspneic and cyanotic
	2 hours, 30 minutes	1.00	5.30	
	2 hours, 20 minutes	5.70	6.07	Animal breathes quietly
475	10 minutes	3.00	6.40	
	25 minutes	3.90	4.70	
	50 minutes	16.70	5.09	Obstructing balloon broke
482	10 minutes	6.1	6.2	
	25 minutes	6.04	6.26	
	40 minutes	6.57	6.49	
	55 minutes	5.41	6.71	
	5 hours, 15 minutes	6.81	6.45	
	6 hours, 15 minutes	5.35	6.97	
	10 hours, 15 minutes	5.81	5.55	

similar conditions by Wolffberg and Loewy and von Schroetter. In table 3 are given the results we obtained on dogs.

The figures in table 3 show clearly that the oxygen and the carbon dioxide of the alveolar air tend rapidly to reach an equilibrium with the gases of the venous blood. Our figures correspond closely to those given by Wolffberg. It must be remembered that the latter represent the dry gases at 0 C.

The figures of Loewy and von Schroetter obtained in the case of a patient, aged 31, with a catheter introduced through a tracheal fistula (case 31) are even closer to ours: before bronchial obstruction oxygen 16.94 per cent, carbon dioxide 3.04 per cent, nine minutes after obstruction, oxygen 6.31 per cent, carbon dioxide 4.47 per cent, twelve minutes after obstruction oxygen 5.55 per cent, carbon dioxide 4.86 per cent.

Furthermore in animals in which gas analyses were performed until complete atelectasis occurred the curves plotted for percentages of oxygen and carbon dioxide show that the percentages vary inversely so

that the curves cross one another (fig 16). The same fact is shown by the figures given by Wolffberg and Loewy and von Schroetter, although it had not attracted the attention of these authors. Later we shall point out the importance of this point for our theory. From the foregoing considerations it is clearly seen that the entrapped alveolus rapidly (in from one to fifteen minutes) undergoes marked qualitative changes, the percentages of oxygen dropping and of carbon dioxide rising, so that their respective partial pressures tend to come into equilibrium with the corresponding gases of the venous blood. These changes occur in exactly the same way in animals as in man.

III *Is Entrapped Air Absorbed, and at What Rate?*—The qualitative changes of the entrapped alveolus entitle us to deduce that quantitative changes in the mass of the gas must simultaneously occur and lead to its total absorption by the venous blood.

TABLE 4—*Figures of Wolffberg*

	Oxygen	Carbon Dioxide
Experiment 2 (Wolffberg)		
Before bronchial obstruction	16.6	28
1 minute after obstruction	4.3	17
2 minutes after obstruction	3.1	19
3 minutes after obstruction	4.1	24
4 minutes after obstruction	3.3	32
5 minutes after obstruction	3.8	30
6 minutes after obstruction	1.6	51*
Experiment 1 (Wolffberg)		
Before bronchial obstruction	16.6	28
2 minutes after obstruction	3.2	31
3 minutes after obstruction	4.2	30
4 minutes after obstruction	5.0	33
6½ minutes after obstruction	2.7	42

\* Dog has dyspnea

In previous communications we have given abundant experimental evidence showing the production of typical atelectasis after complete bronchial obstruction. Roentgenographic, pathologic and histologic evidence has been given by many other investigators as well. A new contribution to this demonstration has been made by our experiments on animals with chests wide open and kept alive in our oscillating negative pressure box. The animal was in this box under conditions ideal for observation. The slightest changes in the physical characters of its lungs—aspect, color and size, could be recorded under direct vision before and after bronchial obstruction. Moreover, although the chest was wide open, the animal was under comparatively normal conditions of respiration because its lungs were submitted to pressure variations exactly equal to pressure variations occurring in its intrapleural cavities before opening of the chest, and the respiration rate in the box was equal to its normal rate.

In our open chest experiments atelectasis usually occurred within from six to ten hours when the animal was able to withstand an experiment of such duration. The succession of events observed in these experiments is as follows. Immediately after successful obstruction

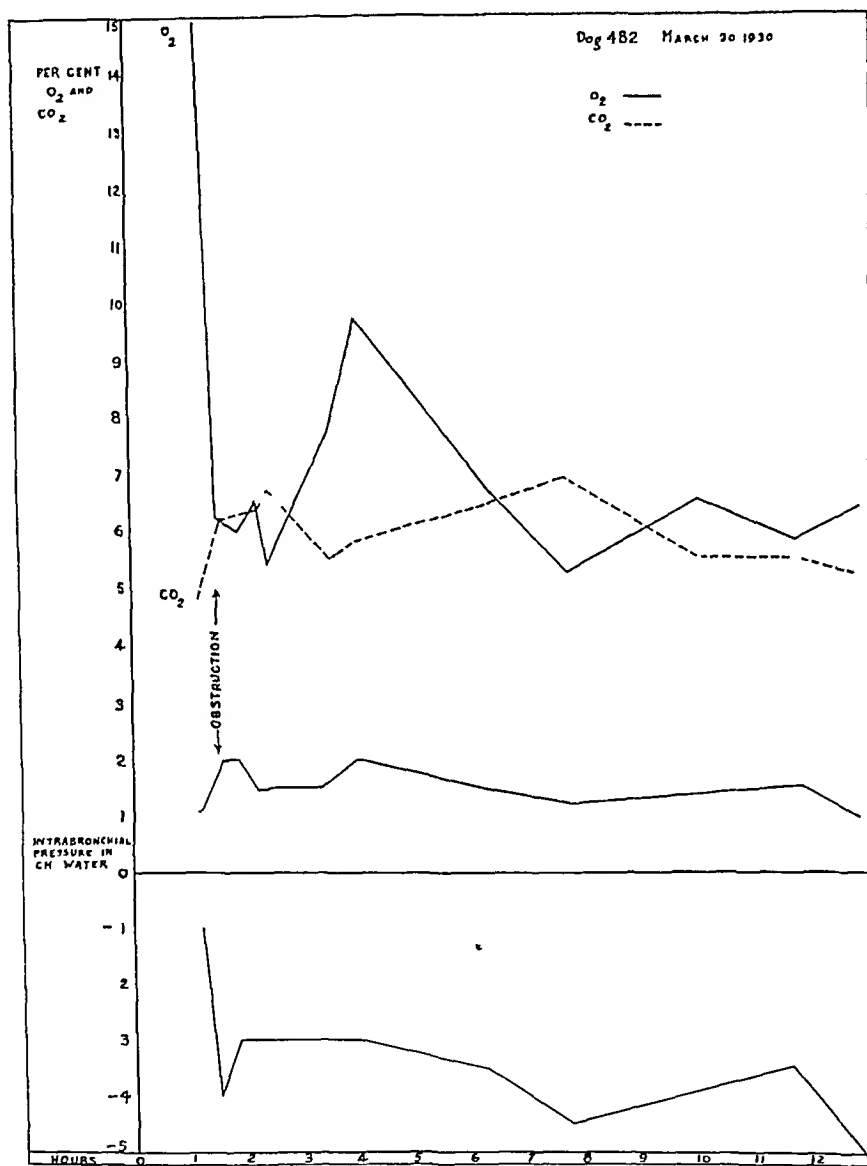


Fig 16—Graphic representation of percentages of oxygen and carbon dioxide obtained by alveolar gas analysis before obstruction and for a period of over twelve hours after obstruction of the right lung. The two lower curves represent the intrabronchial pressure variations in centimeters of water (one-half the actual pressure values, these figures represent the reading of one arm of the manometer)

“the lung stops breathing” whereas the normal lung increases in size. There is a slight inspiratory expansion in the occluded lung owing to the decrease of pressure (increased negative pressure) in the box during inspiration, but it is insignificant as compared to the wide res-



piratory movements of the other lung. Little by little the size of the occluded lung decreases as a whole, without a conspicuous change in its general shape, appearance or color. Gradually it sinks toward the costo-vertebral sinus, whereas the other lung increases in size so that the heart is manifestly displaced toward the obstructed lung. Except for a slight cyanotic hue the obstructed lung does not show any other change until its volume is markedly decreased (to about one-fifth or one-seventh its original size). Then there appear dark bluish-brown patches scattered all over its surface without any special predilection for the hilus or the peripheral portion of the lung. We disagree in this respect with Van Allen and Adams, who claim that atelectasis proceeds from the hilus toward the periphery. We suspect that this happened in their dogs because they permitted a considerable amount of air to be extracted from the obstructed lung. After the great mass of gas is absorbed atelectasis advances rapidly and within approximately an hour is complete. Often small islands of slightly aerated light-colored parenchyma remain on the dark bluish-black atelectatic lung, the complete disappearance of which may take half an hour or more.<sup>3</sup>

That this atelectasis is due to absorption of the alveolar air by the circulating blood is proved by the following data:

(a) If a part of the entrapped alveolar air is aspirated through the cannula, atelectasis will occur more rapidly, the time being inversely proportional to the amount of air extracted.

(b) If the branch of the pulmonary artery corresponding to the obstructed lung is ligated, atelectasis will not occur. As a matter of fact, after this ligation the lung shrinks a little, and after several days becomes quite anless for weeks because of fibrotic contraction, but as Schlaepfer and we have shown the mechanism in this case is altogether different. The fact to keep in mind is, as Lichtheim long ago proved, that obstruction of a bronchus does not lead to atelectasis unless the circulation is intact.

(c) If after atelectasis has occurred we again introduce air into the atelectatic lung, not only does it regain its previous appearance, but also the same cycle of phenomena begins again, namely, qualitative and quantitative changes in the entrapped air and the production of atelectasis in exactly the same length of time if other conditions (general condition of the animal, circulation, respiration, etc.) remain the same.

(d) If instead of air other gases are introduced into the already atelectatic lung, the absorption time is different for each gas depending on their respective coefficients of solubility and diffusion and the chemical affinity for the blood, this will be shown later.

<sup>3</sup> The successive phases of atelectasis have been recorded in a cinematographic film.

(c) If an acute pathologic alteration of the lung endothelium is produced so that the respiratory membrane loses its permeability or the capillaries are damaged, atelectasis does not occur. This is shown in a remarkable way when ether in 100 per cent concentration is introduced into the atelectatic lung. Generally undiluted ether vapor is rapidly absorbed (100 cc in one minute) but it produces a hemorrhagic edema (fig 15) strictly limited to the obstructed portion of the lung. Further introduction of gas in this lung even of carbon dioxide which is usually rapidly absorbed will not be followed by atelectasis. The lung has lost its functional ability for the exchange of gases through the alveolar and capillary endothelium. Production of atelectasis has become impossible. This fact is illustrated in experimental dog 499 (open chest), the protocol of which is given here.

Doc 499—This animal weighed 15 Kg. Fifty-five milligrams of iso-amyl-ethyl barbituric acid per kilogram of body weight was given intraperitoneally.

April 30, 1930, 1:00 p. m. The dog was in the oscillating negative pressure box (oscillations from  $-4$  to  $-8$ ).<sup>4</sup> The oscillation rate was 14 per minute. The heart rate was 116. One-quarter grain (16 mg.) of ephedrine sulphate was given hypodermically. The left lung was obstructed and washed out with oxygen.

4:15 p. m. There was complete atelectasis of the entire left lung.

4:21 p. m. Carbon dioxide was introduced to distend the left lung completely.

4:24 p. m. The carbon dioxide was completely absorbed, and there was total atelectasis.

4:41 p. m. One hundred per cent ether vapor was introduced to distend the lung to the size previously obtained with carbon dioxide (ether vapor was obtained by slowly passing liquid ether through a long metallic coil immersed in water at 90°C).

4:45 p. m. The left lung was edematous, of a dark pink to red color, and increased in size. Absorption was very slow.

4:47 p. m. Oxygen was introduced into the left lung to distend it to its former size.

5:02 p. m. There was no apparent absorption, the volume of the lung was the same.

5:06 p. m. The clamp on the lung catheter was removed. A strong odor of ether came out of the catheter in a forceful stream of gas, the whole amount of oxygen introduced could be withdrawn, showing that no absorption of oxygen and probably of none of the ether had occurred.

Post Mortem. The left lung was pinkish red, in section it was very hemorrhagic and edematous. The weight of the right lung was 140 Gm., of the left (edematous) lung, 232 Gm. Microscopic section showed interstitial hemorrhage (fig 15).

The foregoing data offer indisputable evidence that the alveolar air below a bronchial obstruction is absorbed by the blood circulating

<sup>4</sup> These figures are one-half the actual pressures and represent the readings of only one-half the manometer column.

through the alveolar capillaries, and that its disappearance occurs only in this way

*IV Speed of Absorption of Gases of Alveolar Air Introduced Individually into Atelectatic Lung of Living Animal and Gas Exchange That Takes Place Thereafter*—A series of experiments was performed on dogs with both closed and open chest. In the first series (closed chest), after complete atelectasis of a lung or lobe had occurred following bronchial obstruction (as checked up by roentgenographic examination), oxygen was introduced. After complete atelectasis had occurred again, carbon dioxide was introduced.

This technic is extremely long because atelectasis requires from six to fifteen hours to be completed in the anesthetized animal, besides many animals cannot withstand such a prolonged experiment under deep anesthesia. A much shorter method was therefore devised during our experimentation with the open chest. This consists in aspirating

TABLE 5—*Absorption Times of Oxygen and Carbon Dioxide Individually Introduced in a Lung Previously Rendered Atelectatic*

Dog	Oxygen		Carbon Dioxide		Comment
	Cc	Absorption Time, Min	Cc	Absorption Time, Min	
511	150	15	290	5	Closed chest experiment, roentgenographic control other gases besides oxygen and carbon dioxide were successively introduced
	275	15	275	5	
	280	12	250	7	
507			100	2½	Open chest experiment
504			100	2	Open chest experiment
498	100	11	100	1	Open chest experiment
499	275	1	300	3	Open chest experiment

after obstruction of the bronchus of one lobe, as much alveolar air as possible and washing out the obstructed lobe by filling it with oxygen and emptying it from seven to ten times. In less than thirty minutes the lobe is completely atelectatic. The results obtained by following up the atelectatic lobe filled with oxygen and carbon dioxide are given in table 5. These experiments show that when these gases are introduced separately under atmospheric pressure their respective absorption times vary. What is more, these times are not always the same, varying according to the circulation rate and the permeability of the alveolar endothelium.

The figures in table 5 show that the absorption times of oxygen and carbon dioxide show a constancy which is in agreement with the physical laws of diffusion and solubility. These times, however, vary according to the anatomic conditions of the alveolar endothelium. This fact is well shown in dog 504, in the atelectatic lungs of which were successively introduced in the following order nitrous oxide, carbon dioxide, ethyl chloride, ethylene, carbon dioxide, ethyl chloride, carbon dioxide.

ethylene, oxygen and ether vapor. Because of the lesions of pulmonary endothelium by the gases introduced in it, carbon dioxide at the first introduction was absorbed in two minutes; at the second introduction, in twenty-one minutes; and at the third introduction, in one hour and twenty-two minutes.

Nitrogen when introduced alone under atmospheric pressure into the atelectatic lung was absorbed within sixteen hours in dog 517. It is interesting to point out that whereas such a long time was required for its complete absorption when introduced as the normal constituent of an (i. e., 80 per cent of atmospheric air) it is absorbed on the average in from six to fifteen hours. When pure nitrogen or other neutral gases are introduced into an atelectatic lung, gas analysis of the alveolar content shortly thereafter shows that oxygen and carbon dioxide are present in the same percentage as in the alveolar blood; that is, about 5 or 6 per cent each. From these facts it can be deduced theoretically at least, that when after the introduction of pure nitrogen the oxygen and carbon dioxide have reached these figures, the absorption of the alveolar gases from this point on should proceed at the same rate as if all were now present.

*V. Results Following Introduction of Neutral Gases Separately Into the Atelectatic Lung*—Nitrogen, hydrogen and helium were the gases used in these experiments.

Dog 517 (closed chest experiment)—This animal weighed 11 Kg. Iso-amyl-ethyl barbituric acid anesthesia was used and the left lower lobe bronchus obstructed.

5:30 p. m. The left lower lobe was atelectatic.  
 5:45 p. m. One hundred cubic centimeters of nitrogen was introduced.  
 9:35 p. m. A specimen of gas contained 5.51 per cent oxygen and 7.34 per cent carbon dioxide. The nitrogen was completely absorbed in sixteen hours.

Dog 515 (closed chest experiment)—This dog weighed 12.5 Kg. Iso-amyl-ethyl barbituric acid anesthesia was used. The left bronchus was obstructed.

12:10 p. m. The left lung was atelectatic.  
 12:40 p. m. One hundred and five cubic centimeters of hydrogen was introduced.

4:30 p. m. A specimen of alveolar air contained 6.16 per cent oxygen and 5.03 per cent carbon dioxide.

9:57 p. m. A specimen of alveolar air contained 5.50 per cent oxygen and 6.38 per cent carbon dioxide. The hydrogen was almost completely absorbed in eighteen hours.

Dog 510 (closed chest experiment)—This dog weighed 22 Kg. Iso-amyl-ethyl barbituric acid anesthesia was given. The left stem bronchus was obstructed.

8:30 a. m. Atelectasis was complete. One hundred and seventy-five cubic centimeters of pure helium was introduced into the left lung.

9:30 a. m. Gas analysis showed 5.83 per cent oxygen and 9.34 per cent carbon dioxide.

1:00 p. m. Gas analysis showed 5.34 per cent oxygen and 6.22 per cent carbon dioxide.

2 10 p m Gas analysis showed 5.25 per cent oxygen and 6.64 per cent carbon dioxide. The helium was completely absorbed in twenty-six hours.

Dog 507 (open chest experiment)—The animal weighed 12 Kg. Iso-amyl-ethyl barbituric acid anesthesia was used. The left bronchus was obstructed.

2 00 p m Atelectasis of the left lung was complete. One hundred and fifty cubic centimeters of helium was introduced into the left lower lobe.

2 20 p m Gas analysis showed 2.66 per cent oxygen and 4.54 per cent carbon dioxide.

5 45 p m Gas analysis showed 2.83 per cent oxygen and 5.03 per cent carbon dioxide.

7 52 p m The dog died. Little helium was absorbed.

TABLE 6—*Exchange of Alveolar Gases as Shown by Carbon Dioxide and Oxygen Determinations After Introduction of Various Gases Into an Obstructed Lobe of the Lung*

Gas	Dog	Description	Time	Carbon Dioxide, per Cent	Oxygen, per Cent
Helium	507	Vacuum box experiment, left lower lobe washed out nine times with oxygen and allowed to become atelectatic, 150 cc of helium was introduced into it at	2 00 p m 2 10 p m 5 45 p m	4.54 5.03	2.66* 2.83*
Helium Oxygen	510	Closed chest experiment, the left lower lobe was obstructed and allowed to become completely atelectatic, 200 cc of a mixture of equal volumes of helium and oxygen was then introduced into it at	5 30 p m 8 00 p m	5.86	8.29
Helium		This lobe was now washed out three times with pure helium and 175 cc of helium was introduced into it at	8 30 p m 9 30 p m 1 00 a m 2 00 a m	9.24 6.22 6.64	5.83 5.94 5.25
Hydrogen	515	Closed chest experiment, the left lower lobe was washed out seven times with oxygen and allowed to become atelectatic, then 105 cc of hydrogen was introduced into it at	12 41 p m 4 30 p m 9 37 p m	5.05 6.38	6.16 5.90
Nitrogen	517	Closed chest experiment, the left lower lobe was obstructed and washed out three times with nitrogen by aspiration and distending it with pure nitrogen after each aspiration, then 100 cc of nitrogen was introduced into it at	5 45 p m 9 35 p m	7.34	5.51

\* These are unusually low figures for alveolar oxygen probably due to poor respiration and anoxemia.

We have also introduced various gases into the pleural cavities of dogs and rabbits. In the dog we have not been able to produce a unilateral pneumothorax with air, owing to the permeability of its mediastinum. However, with helium we have been able to produce a temporary unilateral pneumothorax. In the rabbit in which the mediastinum is more like that of man, we have of course been able to produce unilateral pneumothorax with air, nitrogen and helium.

Table 6 is a resumé of these experiments.

The foregoing experiments show that a short while after the introduction of neutral gases into the atelectatic lung oxygen and carbon

dioxide diffuse through the alveolar membrane from the venous blood so that these gases are present in the alveoli under the same partial pressures as in the blood

When a mixture of equal parts of a neutral gas and oxygen or carbon dioxide is introduced into the atelectatic lung the same phenomenon of rapid establishment of gas equilibrium occurs

Doc 510—5 50 p m Two hundred cubic centimeters of equal parts of helium and oxygen by volume was introduced into the atelectatic left lung

7 20 p m Gas analysis showed 5.86 per cent oxygen and 8.29 per cent carbon dioxide

The same modifications in the percentages of alveolar gaseous content occur when more active gases (oxygen carbon dioxide) are introduced individually into the atelectatic lung

Doc 498 (open chest experiment) —This dog weighed 6.5 Kg Iso-amyl-ethyl barbituric acid anesthesia was used The left bronchus was obstructed

10 40 p m One hundred cubic centimeters of oxygen was introduced into the atelectatic lower left lobe

10 50 p m Gas analysis showed 8.59 per cent oxygen and 8 per cent carbon dioxide

VI *Behavior of Respiratory Membrane Toward Anesthetic Gases or Vapors* (Nitrous Oxide Ethylene Ethyl-Chloride, Ether Vapor) —The protocols show the approximate absorption times, by the alveolar endothelium of lungs previously rendered atelectatic of the most usually used anesthetic vapors or gases This question is still under investigation, with the vacuum box method in using lungs previously rendered atelectatic, the absorption time can be checked by direct observation These results will be published later

VII *Changes, if Any, in Intrapulmonary Pressure in Occluded Lung During Process of Gas Absorption* —The prevailing idea concerning the intrapulmonary pressure on the affected side in obstructive atelectasis is that it should be more "negative" than normally because of the shrinkage of the affected lung and the "sucking in" of the other lung heart and diaphragm in the thus liberated space It is generally believed that this negative pressure should increase with the progress of atelectasis, reaching its maximum figure at the completion of atelectasis As a matter of fact we have found no significant changes in the intrapulmonary pressure Figure 17 gives the smoked drum tracings of both the intrapulmonary and intrapleural pressures in dog 422 for a period of over three hours It is seen that these pressures are constant

Loewy and von Schroetter came to similar conclusions after obstructing a bronchus in man "The pressure" they said, 'in the obstructed lung does not show a gradual fall Not only does it remain constant

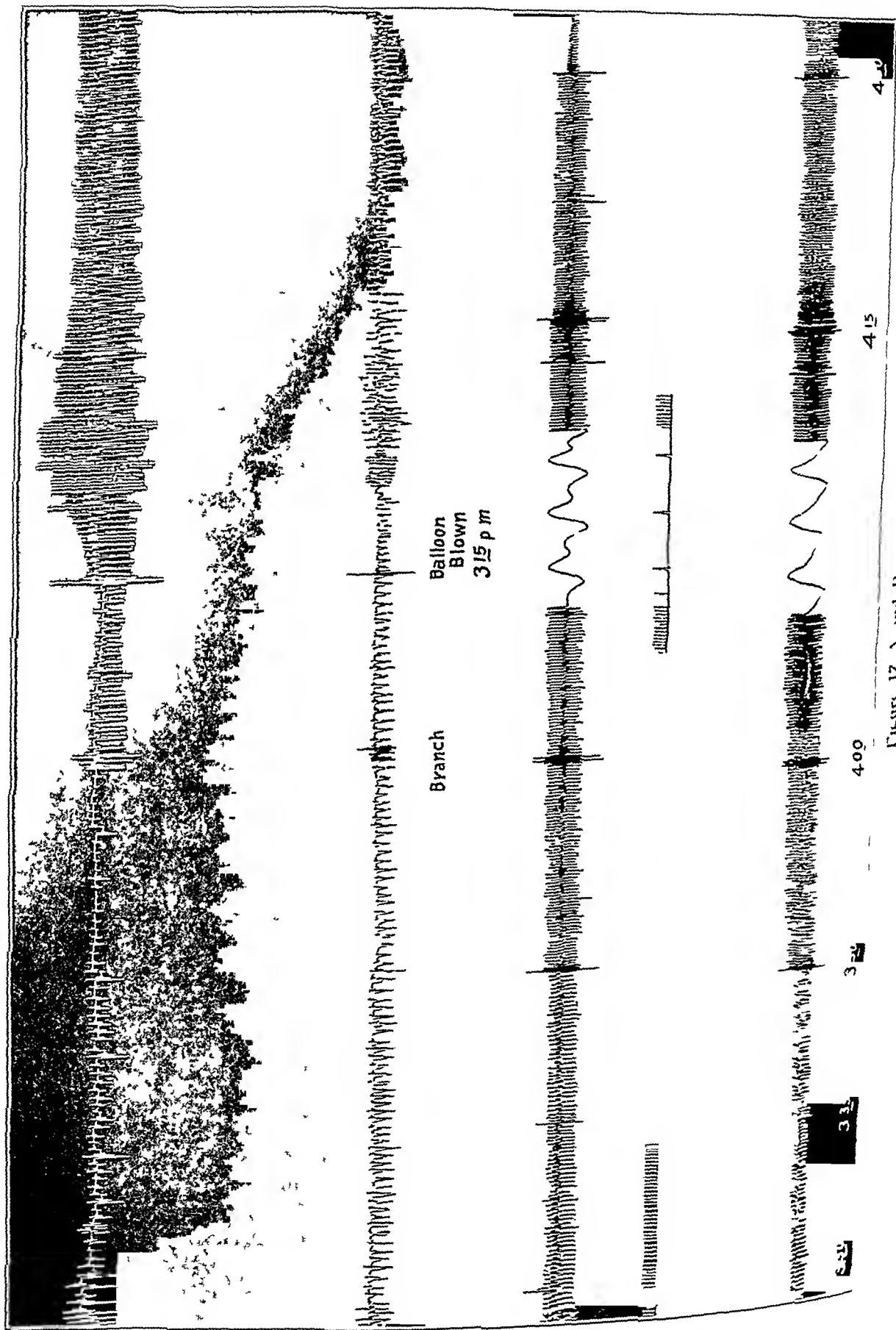


Figure 17 A and B

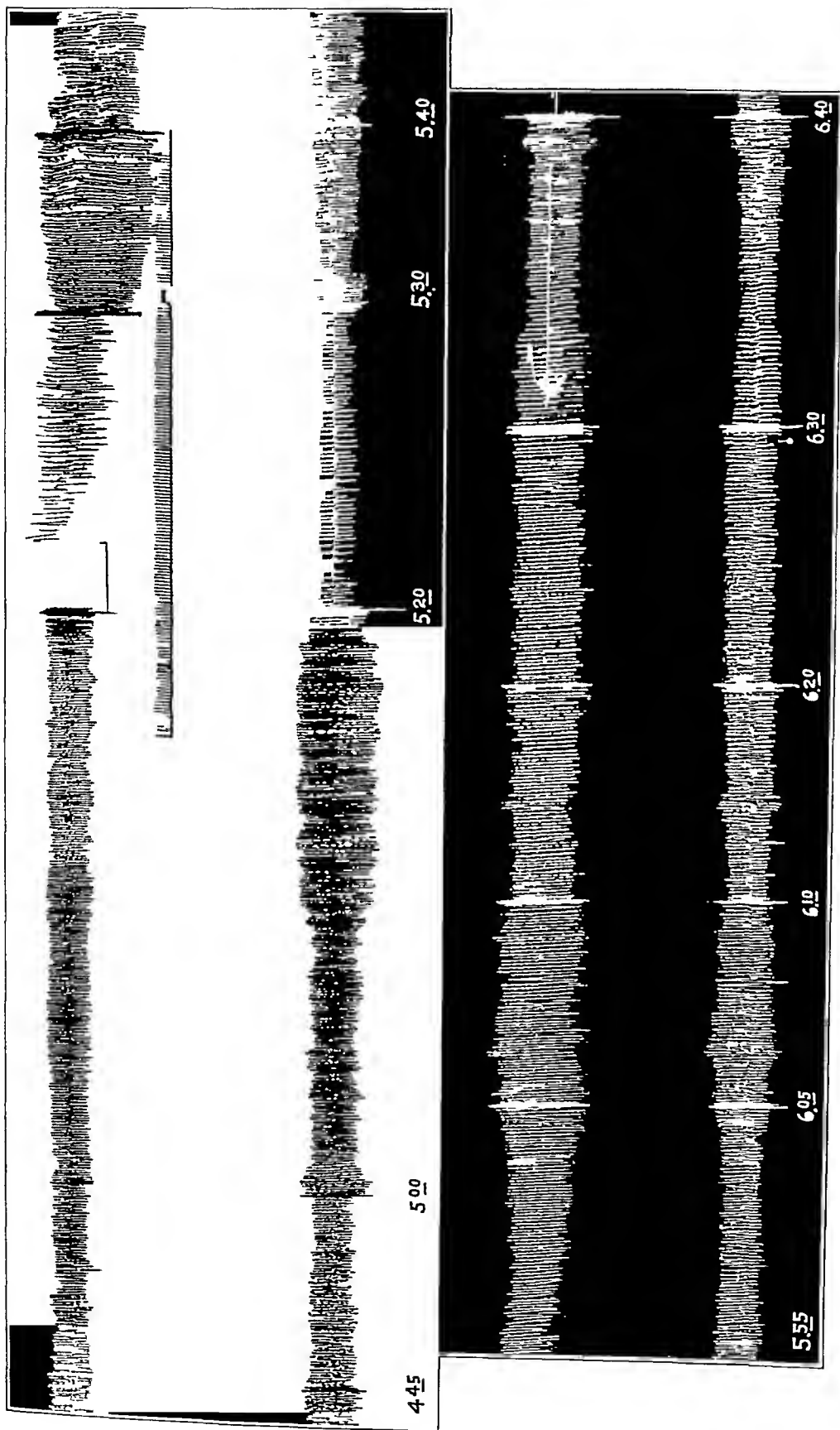


Figure 17 C and D

Fig 17 (log 422)—Obstruction of right lower lobe Parts of a continuous tracing of intrapulmonary and intrabronchial pressures for a period of over three hours An intrapleural cannula was introduced into the right pleura and connected to a mercury manometer recording on a smoked drum (lower curve) The larger tube (intrapulmonary) of the bronchial catheter was connected to another manometer recording on the same smoked drum (upper curve) No changes in pressure occurred for a period of over three hours after bronchial obstruction The arrow indicates time in seconds



but even when relatively large amounts of air, as referred to the total air, are rapidly withdrawn for gas analysis the pressure instantly comes back to normal." They repeated this investigation on four human cases with similar results. These experimental data are only apparently in conflict with the recently reported greatly increased intrapleural negative pressure in cases of atelectasis. We shall discuss this important point under "Comment."

#### OUR THEORY OF PRODUCTION OF ATELECTASIS

The experimental study of the exchange of gases in the obstructed lung leads to the conclusion that the disappearance of alveolar air is due to its absorption by the circulating blood, axiomatically, the reverse seems also true that apneumotosis cannot result unless the alveolar gases are shut off from the external air. In compression atelectasis (pneumothorax, pleural fluid etc.), the collapsed alveolar bronchioles

TABLE 7—Percentages and Partial Pressures of Oxygen, Carbon Dioxide and Nitrogen in Alveolar Air and Venous Capillary Blood

Gas	Alveolar Air		Venous Blood	
	Per Cent	Partial Pressure in Mm Hg	Per Cent	Partial Pressure in Mm Hg
Oxygen	15	114	5	38.0
Carbon dioxide	5	38	6	45.6
Nitrogen	80	608		608.0

become occluded and this occlusion should be complete if atelectasis is to occur. Mere narrowing of the bronchi or bronchioles from whatever cause, cannot produce atelectasis, or, the contrary, it causes emphysema. The foregoing data render possible the elaboration of a theory on the production of atelectasis which is simple, comprehensive and based on such sound physiologic and physical factors as the laws regulating the exchange of gas between alveolar and venous air.

Table 7 represents in round figures the percentages and the corresponding partial pressures of gases in the alveolar and venous air. These differences in partial pressures are possible notwithstanding the continuous exchange of gases through the respiratory membrane only because the alveolar air is continuously renewed by respiration drawing by diffusion on the tidal air filling in each respiration the dead space and bronchi. This exchange is so active that in spite of the continuous renewal of air, the alveolar air is poorer in oxygen and richer in carbon dioxide than the atmospheric air. It is precisely the difference in partial pressures between alveolar and venous gases which render possible oxygenation of the venous blood and elimination of its carbon dioxide.

It is obvious, then, that if a bronchus is obstructed the air entrapped in the lung will undergo qualitative changes. Its composition will gradually approach the percentages of the gases of the venous blood which is constantly coming around the alveoli, carrying away gases which are under excess pressure in the alveoli (oxygen) and giving off gases to the alveoli which it has in excess (carbon dioxide). Such qualitative changes necessarily result in quantitative changes.

In order to simplify the question, we shall graphically represent the alveolus by a circle surrounded by a larger circle which represents the venous blood circulating in the perialveolar capillaries (fig 18). Further, 100 will represent the volumes of a gaseous content of this alveolus. After obstruction of the bronchiolus, an equilibrium of gases inside and outside of the alveolus will be established. We shall consider the three gases separately.

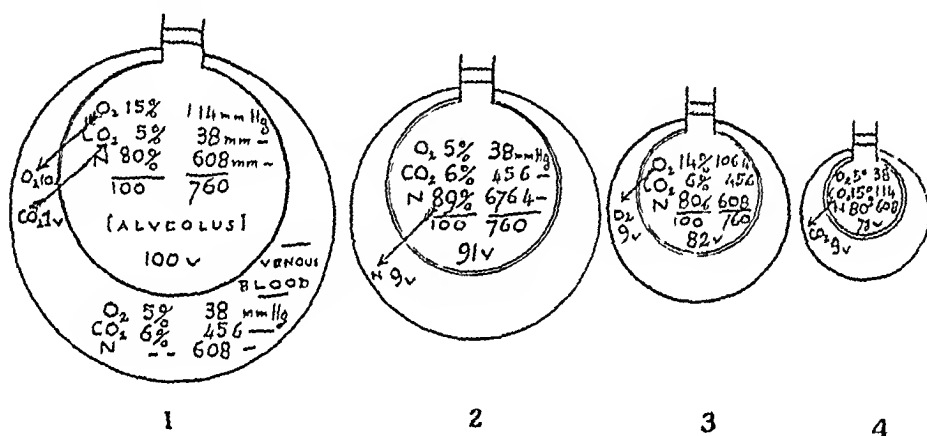


Fig 18—A schematic representation of alveolar gas exchanges, gradual gas absorption and shrinkage of the alveoli after complete bronchial obstruction. The absolute volume of the alveolus is only approximately indicated, but the figures given are relative and demonstrate perfectly well the principles involved. In 1 ten volumes of oxygen diffuse into the venous blood and one volume of carbon dioxide diffuses out of the venous blood into the alveolus. In 2, the alveolus has now lost nine volumes of gas as stated under (1) and the oxygen and carbon dioxide have come into equilibrium in the venous capillary blood and in the alveolus. However, the percentage and partial pressure of nitrogen have now been increased so that nine volumes of nitrogen diffuse out of the alveolus into the venous blood. In 3, nine volumes of nitrogen having previously diffused out of the alveolus into the venous blood, the percentage and partial pressure of oxygen or carbon dioxide have been relatively increased. For purposes of explanation let us say the oxygen has been thus relatively increased in percentage and partial pressure. Nine volumes of oxygen are now ready to diffuse out of the alveoli into the venous blood. In 4 nine volumes of oxygen having diffused from the alveolus into the blood we can now consider that the carbon dioxide in the alveolus is relatively increased by these nine volumes. Thus the partial pressure of this gas is relatively increased and carbon dioxide is ready to diffuse out of the alveolus. Thus the cycle continues until all the gases of the lung are absorbed, although actually the gas exchanges are going on simultaneously and not in the isolated way which we have ideally considered.

Oxygen represents 15 per cent of the gas mixture and it is under a partial pressure of 114 mm of mercury in the alveolus whereas in the venous blood it is present to the extent of 5 per cent and a partial pressure of only 38 mm of mercury (fig 21). Therefore, 10 volumes of oxygen will pass from the alveolus into the blood, at the same time, and for similar reasons, 1 volume of carbon dioxide will pass in the opposite direction from the blood to the alveolus. In this way the gas mixture of the alveolus will lose 9 per cent of its original volume, so that instead of 100 volumes there is now 91 volumes. Now if the alveolar wall were a rigid structure, the total pressure of gas in the alveolus would decrease and instead of a pressure of 114 plus 38 plus 608 = 760 mm of mercury, it would become 38 plus 45.6 plus 608 = 671.6 mm of mercury. Since the alveolar wall is a perfectly elastic structure, it is obvious that under these circumstances the alveolus will retract down for two reasons (1) because of the elasticity of the alveolar membrane and (2) because of the outside intrathoracic pressure. The other lung being in connection with the atmospheric air, the intrathoracic pressure on that side is 760 mm of mercury (the negative intrapleural pressure of from -4 to -7 mm of mercury is comparatively so small that it is of little importance in this mechanism (fig 18)).<sup>2</sup>

We shall now consider nitrogen. At the start, before bronchial occlusion, it represented  $\frac{80}{100}$  of the alveolar gas mixture. Now after the reduction in volume of the gas mixture it represents  $\frac{80}{91}$  of the gas mixture and its partial pressure has risen to 676.4 mm of mercury. But this pressure is much higher than the pressure of nitrogen in the capillary blood, the excess of nitrogen will therefore pass into the blood. In other words, 9 volumes of nitrogen will be carried from the alveolus by the circulating blood, so that the volume of the alveolar air will be  $91 - 9 = 82$  volumes<sup>5</sup> (fig 18).<sup>3</sup>

This decrease in alveolar nitrogen disturbs the equilibrium of oxygen and carbon dioxide between the alveolar air and the venous blood. Now suppose that oxygen alone is affected by this imbalance. It is obvious that instead of 5 per cent, as it was previously it will now represent 14 per cent of the alveolar gas mixture ( $N_2$  80 +  $CO_2$  6 +  $O_2$  14 per cent) and therefore its partial pressure will rise to 106 mm of mercury, so that now again 9 volumes of oxygen are ready to be carried away from the alveolus by the circulating blood. When this happens the volume of the alveolus will decrease to  $82 - 9 = 73$  volumes.

<sup>5</sup> These figures are not, strictly speaking, exact for example  $\frac{80}{91} = \frac{87.9}{100}$  and the partial pressure corresponding to it equals 667.04 mm of mercury. We prefer to give the figures as they are, however because they simplify the explanation without altering any essential relations between the gases.

The carbon dioxide will be affected in the same way (fig 18),<sup>1</sup> and for similar reasons its percentage will rise from 6 to 15 per cent, corresponding to a partial pressure of 114 mm of mercury, so that again 9 volumes of carbon dioxide are ready to be carried away by the circulating blood, thus reducing the volume from 71 to 62. The cycle is repeated, and 9 volumes of nitrogen will be ready to pass from the alveolus into the venous blood. Continuing this series of events, there will be a constant oscillation in gas values and all the alveolar gases will be absorbed. In the open chest experiments we have noted that the initial absorption of gas is slow, after a while the lung seems to shrink much more rapidly, that is, there is an accelerated diminution in the size of the lung. Toward the end of the process when the great

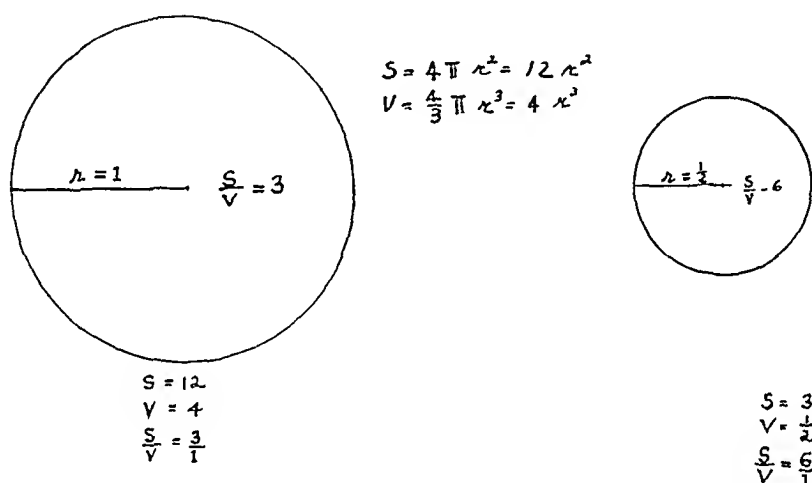


Fig 19—Showing the mathematic acceleration in absorption rate of gases in the alveoli of the lung. These relations probably hold true up to a point where the capillary circulation is definitely impaired.

mass of gas has already been absorbed, the process of absorption seems to slow down markedly, so that one may observe small isolated or patchy areas remaining practically unchanged over a long period of time. This mechanism is explained in figure 19. The alveolus is represented by a sphere the radius of which is 1. The ratio of surface to volume is 3:1. Now suppose gases are absorbed so that the alveolus shrinks and its radius is one-half, the ratio of surface to volume is now 6:1. In other words, the volume of contained gases has been diminished much more than the surface of the alveolus and there is relatively twice as much surface for the contained volume of gas as there was previously. This means that there is more absorbing surface for a unit volume of gas and the alveolus will absorb a greater fraction of its contained volume of gas per unit of time than in the previous

case. Thus with the progressive shrinkage of the lung there is an acceleration in the absorption rate. However, this effect is offset by the impoverishment of the capillary circulation when the alveoli are markedly collapsed, so that in this way we can explain what we have actually observed—a slowing up of absorption toward the end of the process.

It is understood, of course that gas absorption does not occur in the schematic way we have here depicted, actually, there is an incessant simultaneous exchange of all the gases involved. Bohr has shown that extremely small differences in partial pressures are sufficient to insure the diffusion of great amounts of gases through semipermeable membranes. A difference of only 1 mm. of mercury suffices for the passage through the alveolar membrane of the 300 cc. of oxygen per hour per kilogram necessary basically for a man at rest.

We have seen that the anesthetic vapors and oxygen are rapidly absorbed. It is now easy to understand how atelectasis might develop during the course of an operation as in the cases reported by H. Santee and Bergamini and Shepard. Should complete bronchial obstruction by secretions occur during the course of an operation and the lung area involved contain a high percentage of anesthetic vapors and oxygen atelectasis could readily be produced within a short time.

A word should be said further about the rôle played by nitrogen in the gaseous exchanges in the lung. We have seen that it is one of the inert gases, requiring many hours for its absorption. Oxygen and carbon dioxide alone are absorbed by the lung in a relatively few minutes, but when oxygen and carbon dioxide are considered in the atmospheric mixture their absorption periods are greatly prolonged the nitrogen of the air acting as a physical brake by virtue of its slow absorption into the blood. For this reason should bronchial obstruction occur, the time required for the production of atelectasis would be measured in hours rather than minutes. In this way the nitrogen of the air may be considered as a fortunate circumstance of nature to delay alveolar gas absorption and production of atelectasis. This delay is valuable because it allows an interval of time during which re-aeration of the lung could still be easily accomplished. Thus nitrogen may be thought of as the "safety brake" especially during anesthesia and the postoperative period, and may be considered as the "buffer" of the air.

From the foregoing paragraphs it is seen that in the absorption of anesthetic gases and vapors the nitrogen of the air allows their dilution and acts as a mechanical "buffer" delaying their absorption. We think it safe to state that but for the nitrogen of the air, inhalation anesthesia would be so full of danger as to be impracticable.

## COMMENT

There are three possible objections to the theory

1 An equilibrium between the gases of the blood and alveolar blood could be reached after bronchial occlusion, and this should stop further exchange of gases

2 Much more carbon dioxide should pass from the blood into the alveoli, because its speed of passage through the alveolar membrane is thirty times as great as for oxygen, thus atelectasis would be impossible

3 The negative intrapleural pressure has often been reported so great that it should cause a passage of gases from the blood into the alveolus and in this way prevent atelectasis

The first objection can easily be answered. If all the gas molecules are absorbed, this is due to the perfect elasticity of the alveolar membrane and to the great difference in diffusion speeds through it of oxygen, carbon dioxide and nitrogen. For these reasons a perfect equilibrium is never reached, and as Loewy and von Schroetter first showed, the exchange of gases are represented by an asymptotic curve.

The second objection is based on the great speed of passage of carbon dioxide through the alveolar membrane as compared to oxygen or nitrogen. We have already mentioned the experiment of Loewy and Zuntz with the frog's lung demonstrating this point. Exner, using a soap film, showed that carbon dioxide would pass through it toward an indifferent gas with a speed of about 10 cc per minute per square centimeter when under a pressure of only  $\frac{1}{2000}$  of an atmosphere. But the rate of diffusion of gases is regulated by their partial pressures, so that, although carbon dioxide passes rapidly from the blood into the alveolus after bronchial obstruction, an equilibrium is reached when its percentage becomes about 6 per cent in the alveolus, after this point the actual mass of carbon dioxide exchanged through the respiratory membrane is stopped. In other words the exchanges of carbon dioxide are rapidly accomplished, but the actual amount of carbon dioxide passing through the respiratory membrane is regulated exclusively by the differences in partial pressure of the gases respectively in the alveolar and venous air.

The third objection is of even greater importance. Habliston, in 1928 found the intrapleural pressure on the atelectatic side in four cases in man to be —12 —13 —16 and —25 mm of mercury respectively, as against —4 to —7 mm on the unaffected side. Fairis reported two similar cases in which relief was obtained by artificial pneumothorax. Wilson and Gordon (quoted by Habliston) and Ashbury have also reported such cases. Ashbury reported a case with a negative intrapleural pressure of —16 to —20 mm of mercury, after

inducing a partial pneumothorax on the affected side with 600 cc of air, the pressure became  $-4$  to  $-7$  mm of mercury

Presumably, with a negative intrapleural pressure of  $-16$  to  $-20$  mm of mercury the intrapulmonary pressure is also  $-16$  to  $-20$  mm of mercury below atmospheric pressure for the gases in the lung are under a pressure which tends to be equal to the intrapleural pressure

It is interesting to compare these figures to our own data on dogs and the data of Loewy and von Schroetter on man, in which the pressure of the entrapped alveolar air did not change. From the cases of the latter authors it can be deduced that the intrapleural pressure on the affected side also remains constant. The explanation for these discrepancies in the intrapleural pressures between the dog and man is that in the dog both intrapleural pressures are equal because of the elasticity and permeability of the mediastinum. It might be objected that the longest period of bronchial obstruction carried out by Loewy and von Schroetter was only forty-two minutes—a time insufficient for the production of atelectasis.

In the case of a lung which is completely obstructed the pressure of gases within it tends to equal the intrapleural pressure because of the elasticity of the alveoli, thus if the intrapleural pressure were  $-20$  mm of mercury, the intrapulmonary pressure would also be about 20 mm of mercury less than atmospheric, i. e. about 740 mm of mercury. If we consider the percentages of oxygen and carbon dioxide in the entrapped alveolar air as 5 and 6 per cent respectively, their partial pressures would be 38 and 45.6 mm of mercury when the intrapulmonary pressure is 760 mm of mercury and 37 and 44.4 mm of mercury with an intrapulmonary pressure of 740 mm. Therefore, in the case under consideration the effect of a  $-20$  mm negative intrapleural pressure would be to lower the partial pressure of oxygen and carbon dioxide in the alveolus by only from 1 to 2 mm. However it must also be remembered that the gases in the alveolar capillary blood are also subjected to corresponding diminution in their pressures so that from a relative standpoint the partial pressures of the gases in the alveoli and in the alveolar capillaries have not changed. We may thus deduce that the increased negative intrapleural pressure does not materially influence the exchange of gases in the obstructed lung.

So far as the therapeutic effect of artificial pneumothorax is concerned we agree with the foregoing authors quoted as to its palliative effect by decreasing the displacement of the heart but we completely disagree as to its efficacy in freeing the air passages from obstructing material. Pneumothorax cannot further compress a lung already atelectatic. Lastly collapse of the lung by pneumothorax does not favor re-aeration or penetration of air into this lung, on the contrary deeper

respiration by producing dilation of the bronchi is more apt to lead to the formation of airways between obstructing mucus and bronchial wall with subsequent expulsion of the obstacle to respiration

Increased pressure of the entrapped air as produced in coughing or strained respiration would theoretically accelerate the absorption of the alveolar gases, as has been maintained by Van Allen and Adams. We think, however, that these authors have greatly exaggerated the importance of the factor, for an increase in intrapulmonary pressure in the obstructed lung can in these cases be produced only by an increase in the intrapulmonary pressure of the healthy lung. This means an increase in total intrathoracic pressure and consequently in the blood and blood gases as well. It seems that in these cases of Van Allen and Adams, if atelectasis was produced earlier in animals incompletely anesthetized and struggling this was due rather to excessive muscular work and exhaustion of oxygen in the blood while at the same time rapid breathing washed out the carbon dioxide of the blood, the percentages of both gases and their partial pressures in the blood were decreased, causing a more rapid absorption of the entrapped air. We do not think, however, that from their data these authors were justified in coming to the conclusion that "narcotics are advisable because they aid in preventing atelectasis." The chief means the lung possesses to prevent atelectasis or to overcome it once the bronchus is obstructed, is expulsion of the bronchial exudate by cough and deep breathing. Narcotics, on the contrary, deprive the lung of its best means of defense. We believe that for reasons previously described the more efficient treatment (both preventive and curative), besides rolling of the patient from side to side and encouraging him to breathe deeply, is hyperventilation by repeated inhalation of 10 per cent carbon dioxide in oxygen, according to the method introduced by Henderson and Haggard in resuscitation after carbon monoxide poisoning or bronchoscopic aspiration of bronchial exudate.

For a number of years, we have endeavored to show that atelectasis is a well defined clinical syndrome with a definite etiology, pathogenesis, pathology and treatment. It presents various clinical forms which can briefly be distinguished as follows:

1 According to the etiology: obstructive or compressive, postoperative or medical

2 According to its distribution: multilobar (massive), lobar or lobular (patchy)

3 According to its duration: acute or chronic

4 According to its evolution: simple or complicated

The last variety comprises the cases in which infection follows because of the presence of the obstructing agent of microbes of more or



less high virulence so that an infectious process begins in the lung and is favored by the impaired drainage of the respiratory organ. Post-operative atelectasis in which group 4 pneumococcus is always present represents a mild form of infection. Lobar pneumonia, in which more virulent pneumococci are present, represents another type of acute infectious atelectasis occurring as an accident in the course of a pneumococcal bronchitis. Abscess and gangrene of the lung are similarly infectious forms of septic bronchial obstruction and atelectasis, due to specific micro-organisms aerobes and anaerobes. The painstaking work of Smith, Allen, Joannides and others throws a new light on this last variety, justifying our conception.

We have also endeavored to prove that the pathologic process in the different forms of atelectasis develops along the same lines as in similar lesions in glandular organs the ducts of which have been obstructed and to which the lung should be compared. We have shown that the circulation and the ventilation in lungs that have become atelectatic from any cause show exactly parallel changes depending entirely on the condition of the pulmonary ventilation.

The present work by showing the intimate mechanism of the production of apneumotosis, can explain the pathogenesis of the different forms of the disease by sound physiologic principles. It shows further, the importance of physiologic, physical and chemical consideration in the study of respiration in relation to thoracic surgery. Clinical and experimental evidence points to the conclusion that atelectasis is always due to complete bronchial obstruction. We wish to stress the great importance in the pathology of the lung of impairment of free bronchial drainage, and we believe that it has been demonstrated beyond doubt that atelectasis must be definitely associated with the idea of bronchial obstruction. The obstructing agent whatever its nature, should be sought and treatment instituted for its removal and re-aeration of the lung.

#### CONCLUSIONS

1. An experimental method has been devised which gives evidence that when a bronchus is completely obstructed, the entrapped alveolar air rapidly undergoes qualitative and quantitative changes as determined by successive gas analyses.

2. Qualitatively, the percentages and partial pressures of the gases comprising the alveolar air tend to but never quite reach an equilibrium with the gases of the venous blood.

3. Quantitatively, the entrapped alveolar gases pass through the respiratory membrane into the blood circulating in the perialveolar capillaries until complete anoxemia of the involved area is produced.

4 The mechanism of production of atelectasis in the compressed lung (pneumothorax, pleural exudate, intrathoracic tumors, etc) is exactly the same as in bronchial obstruction

5 Besides the gases of the air diffusion of other gases were studied by introducing them into a lung previously rendered atelectatic The different gases used in these experiments were (a) active gases, oxygen and carbon dioxide, (b) neutral gases hydrogen, nitrogen and helium, (c) anesthetic gases or vapors ether ethyl chloride nitrous oxide and ethylene

6 A new experimental method was devised which allows direct vision of the pulmonary changes occurring during the experiment

7 Nitrogen in the respiratory air plays the part of a mechanical "buffer," retarding the absorption of more diffusible and more soluble gases

8 This experimental work has allowed the formation of a theory on the mechanism of atelectasis based on the physiology of exchange of gases in the lung

Mr Eugene Ostrow and Dr Wade Duley gave us technical assistance, Miss Helen C Warny of the Aero-Balloon Corporation, New York City, supplied the helium gas, Mr W S F Dunn and Miss Rosamond McPherson assisted with photographs, Mrs Aies Larsen prepared the histologic sections

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### ABSTRACT OF DISCUSSION

DR W E LEE, Philadelphia When we recently called attention to the unusual incidence of asthma and allergy in patients in whom postoperative atelectasis developed, and suggested that here might be a predisposing factor that would have to be considered, one of our critics accused us of unnecessarily complicating the simple explanation that bronchial obstruction was the only cause of this phenomenon

After hearing this paper by Dr Van Allen and his co-workers, I am sure that every one will feel that he is open to the same criticism He certainly raises doubt as to obstruction being the only cause of atelectasis I think that he presents evidence that this is not a simple problem but a difficult and complicated one

For some time we have been convinced that obstruction is not the only factor concerned, and that it is not the primary etiologic factor but a late determining cause of atelectasis

Dr Van Allen's explanation of the confusing experiences that we have all had with this work—the inconstant results that follow efforts to maintain an airway in the bronchi by coughing and the irregularity with which atelectasis follows bronchial obstruction—requires careful consideration The dependence of the cough reflex and the result of expiratory effort on the presence of what he calls "available air" distal to the obstruction is a new thought In order that an obstruction may be driven away from the periphery by coughing, it is necessary that "available air" be distal to the obstruction to drive it toward the larger bronchi This would fit in perfectly with our claim that it is necessary to maintain or to obtain an airway in the bronchi to prevent or relieve atelectasis This is what we have accomplished in our bronchoscopic drainage in cases of obstruction It is what Santi probably accomplishes when he changes the position of the patients, dislodges the obstructing mass and establishes an airway It is what Gibson in New York probably accomplishes when he thumps and beats his patients, and what Scott, Henderson and Coryllos accomplish when they increase the depth of the respiratory movements by inhalations of carbon dioxide

There is one phase of this work of Van Allen's which has worried me a great deal and that is the question of cough In a previous paper he claimed that in order to produce obstructive atelectasis one must have resisted cough I feel that one should separate cough into two types I fully agree with him that in "unproductive cough," when the obstruction is not relieved, the inspiratory effort which follows the unproductive effort forces, and the negative pressure in the obstructive tissues draws, the obstruction toward the periphery

On the other hand, "in productive cough" there is sufficient air or "available air," as Van Allen calls it, behind or peripheral to the obstruction, to clear the bronchial tubes of the secretions and to maintain an airway and thus allow re-aeration of the lung

Thus Van Allen's demonstration of the presence of "available air" in the pulmonary tissues distal to an obstructed bronchus which comes from the adjacent

alveoli of an unobstructed lobe fits into our clinical observations. In other words, is this not a physiologic provision on the part of nature to provide the adequate "available air" behind or peripheral to obstructing bronchial secretions that makes the productive cough efficient? What would happen to the human race if one did not have a productive cough? I feel that although on first sight this looks entirely at odds with clinical experience, it fits into it very well if one divides cough into two types, as clinicians have done for many years, giving sedatives for the unproductive cough and stimulants for the productive cough.

DR HOWARD LILIENTHAL, New York. I am absolutely unable to criticize or in a scientific way to comment on the excellent demonstrations that you have seen here. I must confess that I was a bit shaken up by Dr. Van Allen's exposure of the apparent impossibility of producing lobular atelectasis by plugging the bronchus. I do know something, however, about what the lung looks like when the chest is opened. I have operated on the chest in suppurative disease. I have operated on it for tumor and for various other conditions exclusive of the empyemas.

I have noticed repeatedly, and I am sure that all of you who have performed operations of this kind must have noticed, that there are occasionally, especially in the lower lobes, spots of atelectasis plainly marked out by pitings several centimeters in diameter, and that these spots of atelectasis are by no means confined to large areas of the lung, but may occur in perhaps fifteen or twenty different places on the surface of the lung and resemble cicatrices. By increasing the intrapharyngeal pressure the lung can gradually be distended, and these atelectatic spots can be blown up to the normal size and color of the lung.

I am not going to try, after what I have heard today, to make any explanations. I shall only say again what I suggested in 1919, after my work at the front during the World War when I performed operations on a good many chests, that this sort of atelectasis, which we at that time called traumatic atelectasis, is probably due to a spasm of the lung, and I see no reason why I should give up that opinion. I believe that a condition inherent in the lung—an idea that some one else hinted at today—produces this form of atelectasis, and not necessarily obstruction of some kind. If there were an obstruction active inflation of the lung would simply accentuate the atelectasis by filling the other parts of the lung and leaving the atelectatic patches because they are obstructed. But they, too, can be blown up, and the lung attains its normal appearance and size.

I offer these remarks simply that Dr. Van Allen and the others who are working on this extraordinarily interesting subject may, if they wish, take this view into consideration.

DR C. M. VAN ALLEN, New Haven, Conn. I should like to leave one idea with you, namely, that atelectasis is complicated. It is not a simple affair of blocking and absorption of air. I heartily agree with Dr. Lilienthal in his remarks and Dr. Lee in regard to the other factors that may probably play an important part. We have reached the stage in our examination of the phenomenon of atelectasis at which we have progressed perhaps about 25 per cent into understanding the various phenomena seen in dogs. We see patchy atelectases develop spontaneously in dogs that have lain under ether anesthesia and to which nothing else happens for three or four hours or longer. There may be other factors (we do not know what they are) that are essential to the production of atelectasis. We know that even in bronchial plugging there are many factors that enter besides those commonly thought simply the absorption of air. Strained breathing greatly accelerates the absorption of air, and even when this breathing is controlled there are still other factors that we do not understand perhaps congestion perhaps inflammation.

In other words, we have dogs in which everything is controlled, the type of respiration, the type of bronchial plug, the position of it, everything we can possibly lay our hands on, and still we find 100 per cent variation in the occurrence of atelectasis, even in the rate of formation

The problem is not solved yet, it is complicated and there is still a lot of work to be done

Perhaps I have an explanation for Dr Lihenthal's observation—I say perhaps because I am not able to say it certainly is so. I have found the same thing in dogs. The patchy atelectasis appears when the lung is inflated and disappears readily. On the other hand, we have found that these patches of atelectasis in dogs, if one carefully explores the bronchial tree with fine scissors and runs down, always have a plug. After you have blown them up the plug is still there. How do they blow up? From intercommunication that exists peripherally from free parts of the lung over in the other parts. The blowing up is very simple. I think that perhaps that is an explanation. I still feel that there may be other explanations for some of these phenomena.

Another point I should like to emphasize is the mechanism of cough. Cough depends on what one might call available air in the lung distal to the plug to remove that plug. That is, if there is no air or if the content of air in that imprisoned part of the lung is lower than in any other part of the lung to a considerable degree, the pressures there are smaller than the pressures elsewhere, and the cough is absolutely unable to evacuate the material. The cough must have a battering ram to use, and that battering ram is the available air in the lung that can be expired, the residual air does the cough no good, it cannot be used by the cough. In other words, if a plug has persisted in the bronchial lumen long enough for the absorption of air to occur to an appreciable degree behind it, then the available air has been lost and the cough can no longer expel or be expected to expel the material unless it gets available air as a result of previous deep inspiration around the peripheral connections. We have seen this occur repeatedly in dogs. We have found that after a partial removal of the air, the air is supplied by the next inspiration, and cough is then effectual in removing the material, so we heartily agree with Dr Lee, Dr Henderson and others who first apply deep breathing as a means of prevention of atelectasis, to allow the lung to aerate itself behind the plug. Dr Lee and his co-workers in their marvelous work on bronchoscopy being done in this city, that of evacuating just one part of the lobe, enter the lobe and free it and allow air to get into the periphery, cough will do the rest. However, do not forget that cough is not the only actor, ciliary action and peristalsis are also concerned. You cannot depend very much on peristalsis, but ciliary action is known to be effectual.

Dr Myerson of Brooklyn has observed blood stains carried from the carina to the larynx in twelve minutes. More recently, Dr Buloway has observed the same thing in the bronchi by roentgenograms, opaque bodies being carried appreciable distances in a few minutes. He calls the action bronchial peristaltic action. I should say that perhaps it was bronchial peristaltic action and perhaps ciliary action. Most patients get well if nothing is done for them. Ciliary action perhaps gets rid of the material the patients do not have to cough to get rid of it.

DR POL N CORYLLOS. Dr Van Allen and his collaborators presented a thorough experimental paper. The passage of air through the interalveolar septums is a fact of great physiologic importance. I do not think, however, that one needs to consider the alveolar "pores" necessary in the physiology of the gas exchange in the lung. In our paper Dr Birnbaum and I discussed this point which

had already been mentioned in a previous paper of Drs Van Allen and Adams. The interalveolar "holes" ("trous d'usure," Letulle) were known and carefully studied a long time ago. The question of their existence has been the topic of heated debate among different investigators. The majority tend to believe that the pores generally occur in the lungs of elderly subjects and that they are the result of a wear and tear process. Whatever they may be, these pores are not essential for the explanation of this phenomenon because the interalveolar septums are perfectly permeable to gases. This can be shown by insufflating 100 per cent ether vapor into the alveoli through the obstructing cannula. The passage of air ceases immediately because of the edema of the interalveolar septums caused by the ether. This explains why patchy atelectasis is possible only in the presence of some degree of inflammatory edema of the alveolar endothelium. In a healthy lung patchy atelectasis would be little short of impossible because exchange of gases continues through the interalveolar septums even when an alveolar duct is completely obstructed.

DR C. M. VAN ALLEN, New Haven, Conn. In answer to the question on lobular atelectasis, I should have gone into that question because it is easily explained. In speaking of the position of the plug of the obstruction, we have spoken of lobular and lobar simply to try to make it simple, but what we really mean is, is the obstruction an isolating obstruction or is it a nonisolating obstruction? An isolating obstruction may be a lobar obstruction or it may be a lobular obstruction in which there is no action of the intercommunicating cores between the two parts of the lung. That may occur readily. We found that these connections between the lobules of the lung function only if a person is breathing normally and deeply, for instance, in a dog that is lying quietly under ether anesthesia, part of the alveoli may be functionless. It is part of nature's method of giving him a margin of safety in his lung. He has too many alveoli for quiet breathing, and after having instituted an obstruction, in such an animal, we find that at first there is no passage of air around through the connections but if the dog then takes a deep breath spontaneously, as they sometimes do after waking after ether and start to breathe deeply, the connections open up, and after that there is free passage of air. Not only physiologic collapse, but exudate, small pneumonic patches, may interfere with such communication from lobule to lobule. If water is injected into the free parts of the lung, the intercommunications can be plugged up, edema in the lung being a common result, associated with the infection that gives rise to bronchial obstruction.

Any of these various factors may interfere with the action of the intercommunications. We are not saying that they operate under all and every circumstance; they operate in a normal lung when the patient is breathing normally and deeply, and therefore we advocate deep breathing for these patients to maintain the patency of the free parts of the lung.

The other point Dr Coryllos made was that he could not repeat my experiments. I can explain that also, I believe. He uses a balloon which when inflated thoroughly seals off the bronchial tree, but in inflation, because of the elasticity of the rubber, it spreads itself along the bronchial lumen for quite a distance and therefore not a lobular but a lobar obstruction has been produced. The balloon spreads itself out over the whole bronchus, so that probably no free passages are left there. I wish that he would get one of my cannulas, which selectively obstruct a given point in a bronchial tree, allowing the bronchial branches proximal to that to remain patent whereas his balloon spreads itself out a long way over the bronchus.



DR F T LORD, Boston I should like to discuss somewhat further the etiology of atelectasis, because running through the meeting this morning is a current of apparent belief that bronchial obstruction is the only cause of this condition, and I cannot believe that the evidence warrants such an assumption. It has long been recognized that there is a type of atelectasis, retraction or compression atelectasis, arising in consequence of encroachment on pulmonary tissue, most commonly observed in connection with the accumulation of fluid or gas in the pleural sac or under the elevated diaphragm. There is no reason to believe that this type of atelectasis is due to bronchial occlusion. The degree of collapse is usually in direct proportion to the amount of encroachment and the physical signs, modified by extrapulmonary fluid or air, are those of solidification of the lung with open bronchi.

There is also a second well established type, obstruction atelectasis, arising in consequence of bronchial occlusion. With this type, the physical signs are dulness, diminished or absent breathing, voice, whisper and tactile fremitus over the involved region, and this combination of signs is quite different from those over collapsed areas with open bronchi.

In our experience, much reliance can be placed on physical signs in the distinction between collapse with open and collapse with closed bronchi. Roentgen examination, though of value for the establishment of atelectasis, cannot often be expected to afford evidence regarding the presence or absence of bronchial obstruction, and even bronchoscopy may fail definitely to answer the question regarding the ingress and egress of air.

Such considerations are of practical importance in the diagnosis of the condition under discussion and have a bearing on the relation of bronchostenosis to lobar pneumonia, during which, to judge from physical signs, the bronchi are usually open. At times, however, with lobar pneumonia and more often with postoperative pneumonia, there is atelectasis with signs of closed bronchus.

It may be that atelectasis arises only under these two conditions, but there is a small puzzling group in which atelectasis complicates pneumonia or infarction, and at autopsy there is no compression from without or bronchial occlusion. In such cases it is difficult to exclude the previous presence of a bronchial plug and the persistence of the collapse of the lung after its disappearance, but it may be that a profound disturbance of local function is also capable of causing atelectasis.

DR POL N CORVILLO Two points have been raised in the discussion of our paper on which I should like to insist. The first is that we should separate "obstructive" from "compressive" atelectasis, and that the latter, "following open or tension pneumothorax or presence of fluid in the pleura, is not produced by the same mechanism." I cannot agree with Dr Lord on this point. On the contrary I believe that, although it might seem paradoxical at first sight the mechanism of production of atelectasis is always the same, namely, bronchial obstruction and absorption of the entrapped alveolar air by the alveolar blood. The factor of the obstruction, although less evident in the compressive than in the obstructive form of atelectasis, is none the less present. In fact the big bronchi may be patent, but the small bronchioles, arteria and ducti alveolares are collapsed. The proof of it is that the simply collapsed but not yet atelectatic lung, as in open pneumothorax, still contains air, and if thrown into water, floats. This shows that notwithstanding the perfect elasticity of the lung, air cannot be completely expelled but it is entrapped in the alveoli because of the collapse and obstruction of the bronchioles. Furthermore, the collapsed lung which at the time of the production of the open pneumothorax was not airless (not apneumotic)

or atelectatic), will become so if the animal survives for the period necessary for the subsequent absorption of the entrapped alveolar air by the mere play of exchanges of gases. Therefore, in compressive as well as in obstructive atelectasis, pneumothorax is produced by exactly the same mechanism.

The second point is that in some cases atelectasis could be produced by bronchoconstriction, as maintained by Dr. Lilienthal. It is, I think, the only point with which I regret to have to disagree with the pioneer of thoracic surgery in this country. I disagree because, as I have already explained, bronchial spasm never produces complete obstruction. In bronchostenosis of any origin, on deep inspiration when the lung expands and the bronchioles dilate, air enters the alveoli, whereas on expiration, and especially in forced expiratory movement, when the lung and bronchioles collapse no air can be expelled (one-way valve). Starling and Jackson have given a clear description of the phenomenon. This is why in all instances in which bronchospasm occurs emphysema and not atelectasis is produced. In allergic asthma in man, anaphylactic shock in the guinea-pig (in which the shock organ is the lung) and in some cases of incomplete bronchial obstruction by foreign body, there is always emphysema and never atelectasis. Furthermore, how can bronchospasm, which is always generalized, explain the lobar distribution of atelectasis and its predilection for the lower lobes or for the lung of the side on which the patient lies? That bronchospasm could be a condition favoring the production of a subsequent complete bronchial obstruction, I would be ready to admit. But even then, why is atelectasis so rare in allergic bronchoconstriction? Wilmer and Lee have lately upheld the thesis that atelectasis is due to allergic bronchospasm. I am afraid that this way we have unnecessarily complicated the question of atelectasis. I think our society will render a real service to the medical profession if we definitely state that atelectasis is always due to bronchial obstruction. The physician should give the patient the benefit of a careful examination, roentgenographic and bronchoscopic. I am convinced that in this way many patients with latent foreign bodies, early tumors, abscesses of the lung or inflammatory bronchiectasis would be treated accordingly.

# AIR IN THE PERITONEAL CAVITY

## ITS EFFECT ON THE POSITION AND ACTIVITY OF THE DIAPHRAGM \*

RICHARD H OVERHOLT, M D

PHILADELPHIA

That pulmonary hypoventilation exists after abdominal operation is a well accepted fact. The alteration in the type of respiration, the limitation of respiratory effort and the sense of thoracic oppression which many of these patients exhibit or complain of are evidence of this fact. Furthermore, a reduction in the vital capacity of patients after abdominal operations has been demonstrated by Churchill and McNeil,<sup>1</sup> Head,<sup>2</sup> Powers,<sup>3</sup> and Muller, Overholt and Pendergrass.<sup>4</sup> This hypoventilation occurs after lower, as well as after upper, abdominal operations but is more marked after the latter. It may result from several factors. Last year Muller, Pendergrass and I<sup>4</sup> reported some observations on the pulmonary status of patients before and after abdominal operations. During this study we observed that postoperatively there occurred an elevation of the diaphragm and a restriction of its activity. Recently Patey<sup>5</sup> also observed a diminution in the movements of the diaphragm after abdominal operations. A comparison of the preoperative and postoperative roentgenograms in his paper shows the diaphragm to be elevated at the time of the postoperative examination. The present studies were undertaken in an effort to ascertain what effect the entrance of air, with the resulting alternation of intraperitoneal pressure, had in this process. I have not found any discussion of the problem of disturbed pressure relationships

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\* From the Department of Research Surgery of the University of Pennsylvania and Surgical Division B of the Hospital of the University of Pennsylvania

1 Churchill, E D, and McNeil, D. The Reduction in Vital Capacity Following Operation, *Surg Gynec Obst* **44** 483 1927

2 Head, J R. The Effect of Operation upon the Vital Capacity, *Boston M & S J* **197** 83, 1927

3 Powers, John H. Vital Capacity Its Significance in Relation to Postoperative Pulmonary Complications, *Arch Surg* **17** 304 (Aug) 1928

4 Muller, G P. Overholt, R H, and Pendergrass, E P. Postoperative Pulmonary Hypoventilation, *Arch Surg* **19** 1322 (Dec) 1929

5 Patey, D H. The Effect of Abdominal Operations on the Mechanism of Respiration *Brit J S* **17** 487, 1930

beneath the diaphragm resulting from the production of a pneumoperitoneum as a factor in the alteration of diaphragmatic position and activity

That the intraperitoneal pressure in the upper part of the abdomen is subatmospheric has been observed by Keppich<sup>6</sup> Melchior<sup>7</sup> and Melchior,<sup>7</sup> Wagoner<sup>8</sup> and Krause.<sup>9</sup> I investigated this subject<sup>10</sup> in dogs using various methods for recording the pressure, and was able to demonstrate a mean subatmospheric pressure in the epigastrium of all animals in the horizontal or head-up position when breathing was quiet. I found that when the closed method for estimating pressures is used, the intraperitoneal pressure decreases during inspiration and increases during expiration. This is contrary to the observation of others who have used an open system. In other words, the subdiaphragmatic and intrapleural pressures fluctuate in the same direction during respiration, and not inversely, as had previously been reported. This would suggest that, normally, free diaphragmatic activity is favored by a subatmospheric pressure in the upper part of the abdomen. It would obviously be more difficult for the diaphragm to contract against a positive intraperitoneal pressure.

#### METHOD

Dogs were used in all of these experiments. They were kept under sodium iso-amyl-ethyl barbituric acid anesthesia throughout the period of the experiment. The drug was given intraperitoneally and in a sufficient amount to drop the respiratory rate to 8 to 10 per minute, the usual dose being 50 mg per kilogram. The position of the diaphragm was determined by making roentgenographic examinations at a uniform distance and exposure with the animal in the horizontal position (fig 1). It was found that the position and contour of the diaphragm could be ascertained more exactly when the exposures were made laterally. A metal pin was inserted into the intraspinous ligament near the level of the dome of the diaphragm in order to provide a fixed point from which to make measurements. Roentgenograms were made during both inspiration and expiration. Errors in the timing of the exposure were minimized by reducing the respiratory rate and by making the exposure in three-twentieths of a second.

In order to check up on the accuracy of this method for determining diaphragmatic position, control animals under sodium iso-amyl-ethyl barbituric acid anesthesia were examined at different times on different days during the

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6 Keppich, J. Intraperitoneal Druck, *Arch f klin Chir* **116** 276, 1921.

7 Melchior, E., and Melchior, P. Intraperitoneal Druck, *Arch f klin Chir* **119** 148, 1922.

8 Wagoner, G. W. Studies in Intra-Abdominal Pressure, *Am J M Sc* **171** 697, 1926.

9 Krause, N. J. Der intra-abdomineller Druck im Bereiche des Subdiaphragmalraumes und Epigastriums und dessen Bedeutung in der Magen Chirurgie, *Arch f klin Chir* **144** 201, 1927.

10 Overholt, R. H. Observations on Intraperitoneal Pressure, *Arch Surg*, to be published.



Fig 1—Lateral roentgenograms made before (A) and after (B) laparotomy on dog weighing 10 Kg, with uniform position, distance, exposure and respiratory phase. Illustrates method of studying position of diaphragm. Notice clearcut diaphragmatic shadow throughout. Metal marker and thoracic vertebra used as fixed points in making tracings. Elevation after laparotomy was 17 cm. Diaphragmatic excursion before laparotomy was 12 cm, and after laparotomy, 0.6 cm.



Fig 2—Superimposed tracings made from roentgenograms of two of the control animals. These experiments test the accuracy of the method of measuring changes in the position of the diaphragm. At left, superimposed tracings of roentgenograms made on the same animal on different days, the exposure being made during inspiration. At right, tracings made one hour apart, both exposures during expiration. Note the similarity of these tracings.

same phase of respiration. Tracings made of these roentgenograms and superimposed on each other showed the diaphragm to be in approximately the same position in each exposure (fig 2). No animals were used in these experiments in which the breathing was fast and difficult to follow. Often several roentgenograms were taken during the same phase of respiration in order to check the accuracy of the timing.

In seventeen animals pneumoperitoneum was induced by injecting air in amounts varying from 10 to 100 cc per kilogram of body weight. In seven animals, studies were made before and after a laparotomy had been performed. Diaphragmatic position and the extent of diaphragmatic excursions were determined by superimposing tracings of the roentgenograms made during inspiration and expiration before and after the pneumoperitoneum had been induced.

Changes in the movements of the diaphragm were observed fluoroscopically and recorded in eight animals before and after the injection of air into the

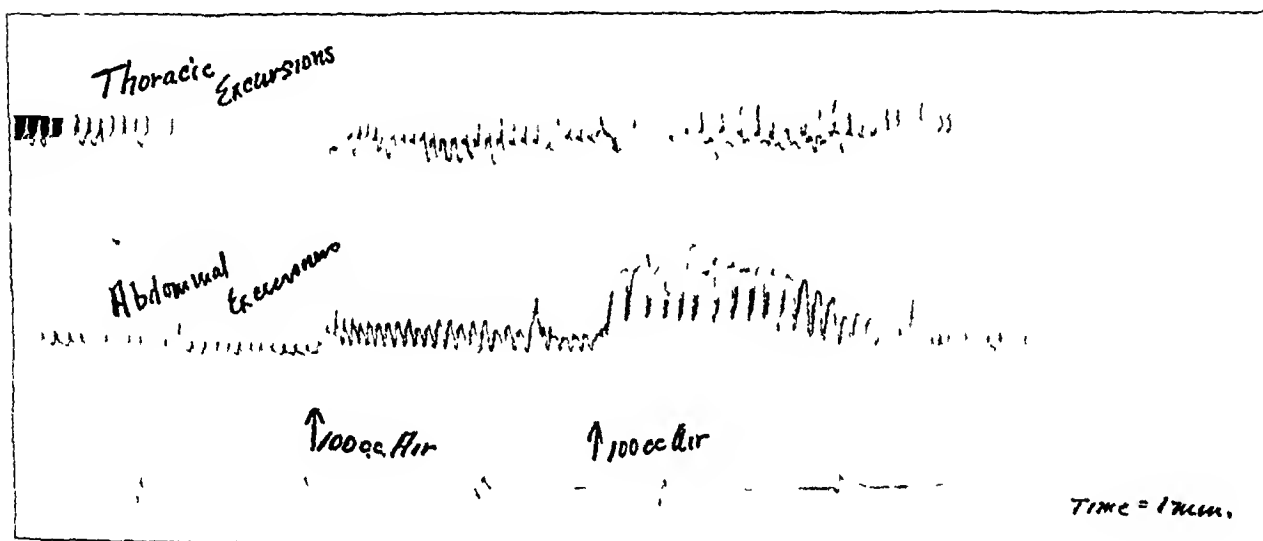


Fig 3—Kymographic tracing showing the effect of the injection of 100 cc of air (10 cc per kilogram) at two different times on the character of thoracic and abdominal respiratory movements. Note that the increase in the rate lasted for only three or four minutes.

peritoneal cavity. In three animals, after the injection of air, the fluoroscopic examinations were repeated every forty-five minutes for a period of three hours.

In five animals kymographic tracings of abdominal and thoracic respiratory excursions were recorded before, during and after the injection of air into the peritoneal cavity. Immediately following the injection of air, the respiratory rate increased for a short interval and then dropped back to, or nearly to, its previous rate. This effect is shown in figure 3. For this reason, all roentgenographic studies were delayed until after the respiratory rate had returned to its original level.

#### RESULTS

Following the injection of air into the peritoneal cavity, or after laparotomy, two changes in the diaphragm were observed. In every animal studied an elevation and a diminution in diaphragmatic excursions were noted.

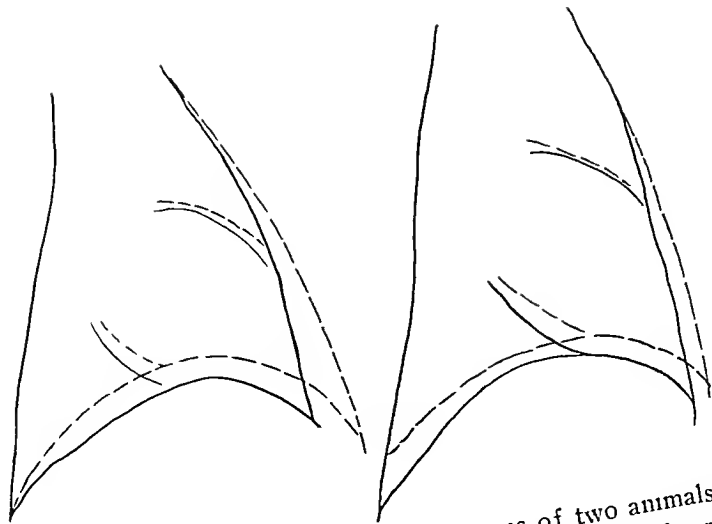


Fig 4—Superimposed tracings of roentgenograms of two animals made during expiration before (solid line) and after (dotted line) 50 cc of air per kilogram had been injected intraperitoneally Note change in position of diaphragm, thoracic cage and heart

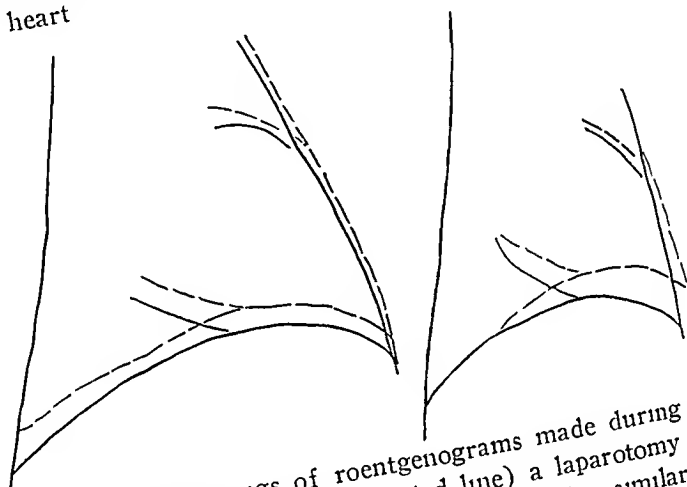


Fig 5—Superimposed tracings of roentgenograms made during inspiration in two dogs before (solid line) and after (dotted line) a laparotomy had been performed Note changes in position of diaphragm and also similarity to changes induced by injection of air as shown in figure 4

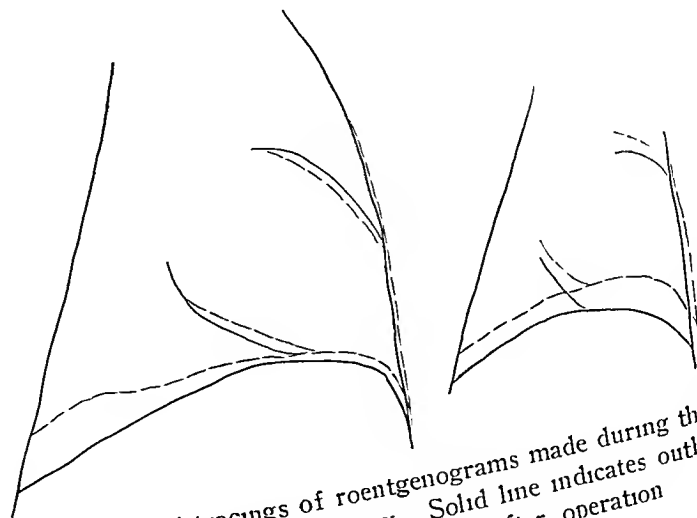


Fig 6—Superimposed tracings of roentgenograms made during the same phase of respiration before and after laparotomy Solid line indicates outline of thorax before operation, dotted line, outline of thorax after operation

The upward shift of the diaphragm could be easily demonstrated when the preoperative and postoperative films made during similar phases of respiration were compared. The degree of the elevation varied from 0.3 to 1.8 cm., the average for the animals given the injection



Fig. 7—Superimposed tracings of roentgenograms made during both phases of respiration both before and after laparotomy. Solid line indicates position of diaphragm during expiration, dotted line position during inspiration. Note the extent of diaphragmatic movement before, and the limitation after. Iso-amyl-ethyl barbituric acid anesthesia was used.

TABLE 1—*Diaphragmatic Elevation in Twenty-One Dogs (Average Weight, 6.7 Kg.) Under Iso-Amyl-Ethyl Barbituric Acid Anesthesia*

	Number of Animals	Elevation, Cm		
		Inspiratory Phase	Expiratory Phase	Average
After laparotomy	7	0.98	1.1	1.02
After pneumoperitoneum	14	1.4	1.4	0.96

TABLE 2—*Diaphragmatic Movement in Fifteen Dogs (Average Weight, 8.6 Kg.) Under Iso-Amyl-Ethyl Barbituric Acid Anesthesia*

	Cm
Normal excursion (6 animals)	1.3
After laparotomy	0.57
Normal excursion (9 animals)	0.69
After pneumoperitoneum	0.35

tion being 0.958 cm., and that for the animals undergoing laparotomy, 1.02 cm. The extent of the elevation depended more on the size of the animal than on the amount of air injected per kilogram of body weight, e.g., after the intraperitoneal introduction of 100 cc. of air per kilogram the diaphragmatic elevation during expiration for a dog weighing 3.5 Kg. was 0.4 cm., whereas in an animal weighing 6 Kg. the elevation was 1.6 cm.



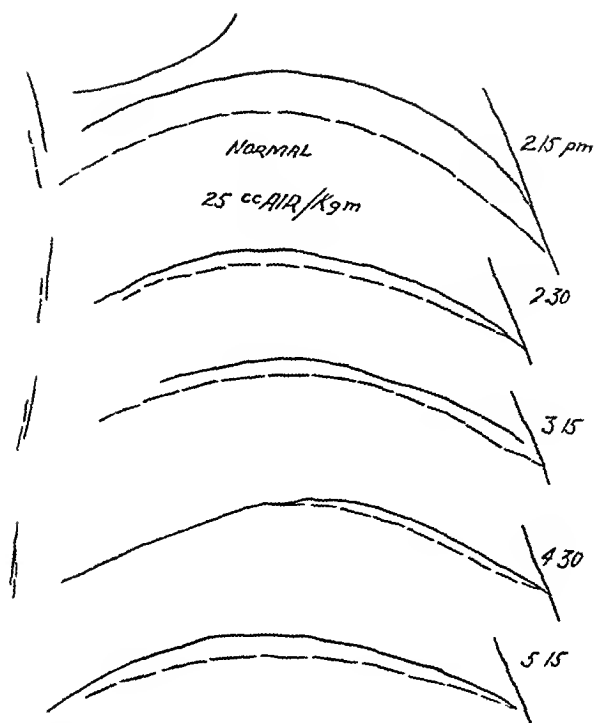


Fig 8—Tracings made on the fluoroscopic screen of diaphragmatic excursion before, and at intervals of forty-five minutes after the intraperitoneal injection of 25 cc of air per kilogram. Solid line indicates diaphragmatic position during expiration, dotted line, position during inspiration. Note definite limitation of excursion of diaphragm which was maintained over a considerable period of time.

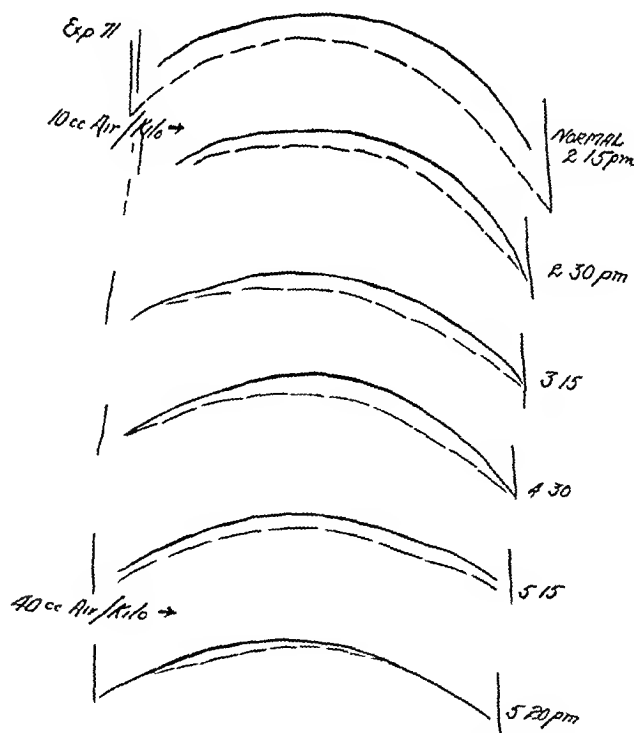


Fig 9—Tracings from fluoroscopic screen of diaphragmatic movements under normal conditions and after the intraperitoneal injection of 10 cc of air per kilogram. Solid line indicates diaphragmatic position during expiration, dotted line, position during inspiration. The reduction of the excursions is noticeable. At the conclusion of the experiment, 40 cc more air per kilogram was injected and the diaphragmatic action was further restricted.

The greatest change in the position of the diaphragm took place in the posterior portion. The triangle formed by the border of the heart and the posterior costophrenic angle was diminished in size. The outlines of the bronchi in this area were changed by the retraction of the lung following elevation of the diaphragm. An increase in the size of the thoracic cage was noted, the heart assumed a higher position, and its axis was slightly altered in all of the animals studied (figs. 4 and 5).

A reduction in the extent of the diaphragmatic excursion in animals under iso-amyl-ethyl barbituric acid anesthesia was noted in each instance after the production of a pneumoperitonium (fig. 6). Under the fluoroscope, injections of from 10 to 100 cc. of air per kilogram caused approximately a 50 per cent decrease in the amplitude of the excursion (figs. 7 and 8). This effect was noted over a period of three hours. After laparotomy in every animal a similar reduction in movement was demonstrated.

#### COMMENT

These observations indicate that the entrance of air into the peritoneal cavity may be responsible in part for the reduction of pulmonary ventilation by causing elevation and partial limitation of the motion of the diaphragm. The alteration of position and the restriction of activity of the diaphragm may be the result of a change in the intraperitoneal pressure. Under these conditions the diaphragm must move between a positive intraperitoneal and a subatmospheric or negative intrapleural pressure. That the normal pressure relationships in which the diaphragm functions are disturbed after the sealed intraperitoneal space is opened is suggested by the similarity of the results in the injection and laparotomy series. Furthermore, once it has been established that the mean intraperitoneal pressure in the upper part of the abdomen is subatmospheric, it is obvious that an opening of this sealed cavity would cause a change in the pressure in the subdiaphragmatic region.

Two explanations for the fact that variations in the amount of air injected failed to show corresponding elevations in the diaphragm can be given. 1. In previously reported work,<sup>10</sup> it was shown that the intraperitoneal pressure changes immediately from a subatmospheric level to a positive level following small injections of air, but fails to show a corresponding rise on further injections because of the elasticity of the abdominal musculature. This was also pointed out by Coombs<sup>11</sup> in observations on animals after intraperitoneal injections of saline solu-

11 Coombs H. C. The Mechanism of the Regulation of Intra-Abdominal Pressure. *Am J Physiol* **61** 159, 1920.

tion 2 The structural limitations of the diaphragm itself and the attachment to the costal arch tend to prevent elevation of the diaphragm

No attempt has been made to attribute all of the diaphragmatic restriction after laparotomy to the presence of air in the peritoneal cavity. It is realized that pain at the site of operation, reflex splinting of the abdominal musculature, distention of the bowel and the application of abdominal binders or dressings also play a rôle in this process.

#### CONCLUSIONS

The position and mobility of the diaphragm were studied in animals under sodium iso-amyl-ethyl barbituric acid anesthesia. It was observed that following the introduction of air into the peritoneal cavity, either by injection or as a result of laparotomy, the diaphragm assumed a higher position and its excursions were definitely restricted.

Dr V C Johnson of the Department of Roentgenology of the Hospital of the University of Pennsylvania assisted in the fluoroscopic work in this study.

# ESOPHAGUS, STOMACH AND HEART FOLLOWING UNILATERAL PHRENICECTOMY<sup>1</sup>

H C BALLON, M D

H M WILSON, M D

J J SINGER, M D

AND

B A GRAHAM, M D

ST LOUIS

That phrenicectomy has a place in the treatment for certain diseases of the lungs would appear to be a more or less accepted fact. In the past, practically all observations in this connection have dealt with the immediate or remote effects of phrenicectomy on a diseased portion of the lung and on the lung as a whole, and justly so, for this is undoubtedly the chief consideration.

We observed gastro-intestinal symptoms in a few patients following phrenicectomy. In one instance the so-called condition of "cardio-spasm" supposedly developed following this procedure. We therefore deemed it advisable to study the relationship of the diaphragm to the esophagus both before and after phrenicectomy. The occurrence of certain cardiac symptoms in some of these patients following phrenicectomy also led us to make electrocardiograms before and after the operation.

We have divided our paper into three parts, the first dealing with changes in the esophagus of patients following phrenicectomy, the second with changes in the esophagus of dogs following phrenicectomy, and the third with the electrocardiogram of patients before and after phrenicectomy. The clinical observations were all made on patients in the chest service of Barnes Hospital.

## ANATOMIC RELATIONSHIPS OF THE ESOPHAGUS TO THE DIAPHRAGM

The anatomy of the lower end of the esophagus has been thoroughly studied by Mosher<sup>1</sup> and by Mosher and McGregor<sup>2</sup>. Particular atten-

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\* From the Departments of Surgery and Internal Medicine, Washington University Medical School, and the Chest Service, Barnes Hospital.

1 Mosher, H. P. Liver Tunnel and Cardiospasm, *Laryngoscope* **32** 348, 1922, Cardiospasm, *Pennsylvania M. J.* **26** 240, 1923, Findings with the Barium Bougie in Cardiospasm, *Ann. Otol., Rhin. & Laryng.* **36** 1127, 1927, The Lower End of the Oesophagus at Birth and in the Adult, *J. Laryng. & Otol.* **45** 161 (March) 1930.

2 Mosher, H. P., and McGregor, G. W. Study of Lower End of the Oesophagus, *Ann. Otol., Rhin. & Laryng.* **37** 12 (March) 1928, Study of Lower End of Oesophagus, *Tr. Am. Laryng., Rhin. & Otol. Soc.* **34** 294, 1928.

tion has been paid to the crural fibers and to their formation of a muscular sling about the lower end of the esophagus. The diaphragm, which is a dome-shaped musculomembranous sheet, receives its motor innervation from the phrenic nerves. The sympathetic fibers to the diaphragm are tropic while the vagus takes no part in its innervation. The intercostals send sensory fibers to the diaphragm.<sup>3</sup> The esophagus pierces the diaphragm by passing through the muscular hiatus esophagus. It runs obliquely to the left as it passes through the hiatus at the level of the tenth dorsal vertebra and thence continues very obliquely to the left into the stomach. The abdominal portion of the esophagus or epicaardia is from about 2 to 5 cm. in length (Carman,<sup>4</sup> Imperatori<sup>5</sup>). Physiologic narrowing of the lower part of the esophagus occurs at the hiatus and at the cardiac opening. Much attention has been directed to these two points in discussions on "cardiospasm."

The structure and position of the diaphragmatic crura seem to constitute a perfect mechanism for pinching shut the esophagus at this point. Jackson<sup>6</sup> suggested that the barrier to regurgitation which can automatically open at the approach of a bolus of food is located at the diaphragm and is due to two mechanisms: (1) the normal kinking of the abdominal part of the esophagus, and (2) the diaphragmatic pinchcock. Joannides<sup>7</sup> observed two types of contraction in the lower part of the esophagus of the anesthetized dog. By inserting a finger into the esophagus through a gastrostomy opening he could produce a circular constricting "esophageal" contraction as a result of stimulation of the peripheral end of the vagus or of the esophagus at any level above the gastro-esophageal junction. A second type of contraction was coincident with each inspiration and was apparently due to contractions of the diaphragmatic pillars. This "milking action" was also observed following stimulation of the trunk or branches of the phrenic nerve in the immediate vicinity of the pillars. Sauerbruch<sup>8</sup> noted that the resistance felt by a finger introduced into the esophagus through a gas-

3 Kiss, F., and Ballon, H. C. Contribution to the Nerve Supply of the Diaphragm, *Anat. Rec.* **41**: 285 (Feb. 25) 1929.

4 Carman, Russell D. The Roentgen Diagnosis of Diseases of the Alimentary Canal, ed. 2, Philadelphia, W. B. Saunders Company, 1920.

5 Imperatori, C. I. Cardiospasm, *Arch. Otolaryng.* **11**: 178 (Feb.) 1930.

6 Jackson, Chevalier. The Diaphragmatic Pinchcock in So-Called "Cardiospasm," *Laryngoscope* **32**: 139, 1922.

7 Joannides, M. Influence of the Diaphragm on the Esophagus and on the Stomach, *Arch. Int. Med.* **44**: 856 (Dec.) 1929, The Relation of the Hiatus Oesophageus of the Diaphragm to the Stomach, *ibid.* **43**: 61, 1929.

8 Sauerbruch, F. Chirurgie der Brustorgane, Berlin, Julius Springer, 1925, vol. 2. Sauerbruch, F., and Haecker, R. Zur Frage des Cardiaverschluss der Speiseröhre. *Deutsche med. Wchnschr.*, Aug. 2, 1906, no. 3.

triotomy opening and attributed by him to the sling of the diaphragm disappeared following section of both phrenic nerves

It is obvious from such experiments that there exists a close relationship between the normal diaphragm and esophagus. It is therefore of interest to determine the effect of a high insufficient diaphragm on this relationship

#### EFFECTS OF INSUFFICIENCY OF THE DIAPHRAGM

Following phrenicectomy the diaphragm on the same side becomes paralyzed, atrophic and elevated and usually shows a paradoxical movement on respiration. Conditions similar in every respect have been found in certain cases of eventration or "insufficiency" of the diaphragm. It is therefore advisable to consider cases of eventration.

Lerche<sup>9</sup> advised the term "insufficiency" rather than eventration for the condition in which an abnormally high leaf of the diaphragm, usually the left, forms a sacklike dilatation into which one or more of the abdominal organs, especially the stomach, colon or even the spleen, are displaced upward. The various causes ascribed to this condition are congenital atrophy, dystrophy, neuromuscular degeneration following injury, neuritis or other involvement of the phrenic nerve or its fibers, certain infectious diseases and changes in the musculature of the diaphragm such as pseudohypertrophic lipomatosis and myositis.

Acute insufficiency of the diaphragm has been observed following one of the infectious diseases. After a few weeks the diaphragm returns to its normal level, and all symptoms disappear.<sup>9</sup>

Chronic insufficiency of the diaphragm includes those cases in which there is a permanently elevated diaphragm. Patients with this condition may be singularly free from symptoms for a considerable period.<sup>9</sup> They may, however, have sensations of heaviness in the epigastrium and may also be troubled with dysphagia or gaseous eructations (Dillon<sup>10</sup>). They may also complain of dyspnea on exertion. In such cases of eventration one finds a permanently large stomach bubble under the highly arched diaphragm which may even be at the level of the third interspace.

Hitzenberger<sup>11</sup> stated that in the case of a high left diaphragm the pars cardiaca is displaced upward and dorsally, the lower end of the esophagus craniodorsally instead of caudoventrally. This causes an angulation of the esophagus which he believed may be responsible for

<sup>9</sup> Lerche W. Insufficiency (Eventration) of the Diaphragm. *Surg Gynec Obst* 34:224, 1922.

<sup>10</sup> Dillon J. Die Beziehungen zwischen Zwerchfellfunktion und Verdauungs-krankheiten. *Arch f Verdauungskr* 42:685, 1928.

<sup>11</sup> Hitzenberger K. Das Zwerchfell. Vienna: Julius Springer, 1927.

the so-called "dysphagia paradoxa" It is called paradoxical dysphagia, because such patients are able to swallow solids better than liquids, and because they fail to lose weight Eppinger<sup>12</sup> stated that in the case of a diaphragm high on the left side the greater curvature of the stomach comes to lie anteriorly and superiorly while the lesser curvature lies inferiorly and posteriorly The duodenum is also displaced Lerche<sup>9</sup> reported somewhat similar observations in a case of eventration of the diaphragm There was angulation of the abdominal portion of the esophagus as it entered the elevated cardia and rotation of the stomach so that the greater curvature pointed directly forward Esophagoscopy examination in this instance confirmed the observation of increased angulation of the abdominal part of the esophagus to the left The patient swallowed a tube filled with barium sulphate Under the fluoroscope it was observed that the esophagus turned upward into the fundus at a more acute angle than is usually seen

Hitzenberger<sup>11</sup> also stated that in the case of a diaphragm high on the right side the pylorus may come to occupy such a position as to make the longitudinal axis of the stomach lie transversely

Such definitely disturbed relationships between the esophagus and the stomach in cases of eventration of the diaphragm warrant even more careful consideration of the effects of phrenicectomy

#### LITERATURE NOTING GASTRO-INTESTINAL SYMPTOMS FOLLOWING PHRENICECTOMY

Hecht<sup>13</sup> noted that some of his patients complained of a feeling of fulness after a large meal the first few days following phrenicectomy He observed one patient with such complaints which persisted for a few weeks following a right-sided phrenicectomy

Maendl and Schwarzmann<sup>14</sup> reported their experiences in 100 phrenicectomies Almost all their patients the left side of whose diaphragms were paralyzed suffered from loss of appetite, a feeling of fulness and vomiting directly after the operation, which was performed under local anesthesia

In reporting 300 phrenicectomies Welles<sup>15</sup> stated that in a small number of cases the rise of the diaphragm was followed by digestive upsets The majority of these were temporary and were no more common following left-sided than following right-sided phrenicectomy

12 Eppinger K, quoted by Hitzenberger (footnote 11)

13 Hecht, P Phrenicuschirese und gastrokardialen Symptomkomplex, Beitr z Klin d Tuberk **70** 336, 1928

14 Maendl, H, and Schwarzmann, E Unsere Erfahrungen bei 100 Phrenicectomien, Beitr z Klin d Tuberk **71** 80, 1929

15 Welles E S Phrenicectomy in Three Hundred Cases of Pulmonary Tuberculosis Arch Surg **19** 1169 (Dec) 1929

Uebelhoei<sup>16</sup> reported an example of *relaxatio diaphragmatica* following a left-sided phrenicectomy on a woman, aged 24, with pulmonary tuberculosis and cavitation. This case was reported in 1928, and the operation was performed in October, 1924. This patient had had some obstipation and vomiting before the operation. These symptoms were markedly increased following the phrenicectomy. There was no cardiac displacement. The patient did not complain of palpitation. The condition after the phrenicectomy suggested either a relaxed diaphragm or a diaphragmatic hernia. Sauerbruch<sup>8</sup> operated on the patient, found a relaxed diaphragm and plicated it, the patient was relieved of her symptoms. The diaphragm was found at the level of the fourth rib. The authors stated that they never observed an elevation of the diaphragm after phrenicectomy above 8 to 9 cm. on the left or above 12 cm. on the right. They stated that the following considerations arose in their case, which is the only one observed in a personal series of 1,000 phrenicectomies. 1. The shrinking lung may have pulled the diaphragm with it, since the wall of the chest and the mediastinum were unyielding because of adhesions. 2. A coexisting meteorism expressive of an increased intra-alimentary pressure forced the diaphragm up higher than usual. This is in accord with the views of Assmann<sup>17</sup>. 3. There may have been a congenital basis, that is, a preexisting weakness of the diaphragm.

#### THE EFFECT OF PHRENICECTOMY ON THE ESOPHAGUS

We examined twenty-seven patients before and after phrenicectomy. Fluoroscopic and roentgen examinations of the esophagus and stomach with the use of an opaque meal consisting of a thick mixture of barium sulphate and water were made. Five of the twenty-seven patients whom we examined complained of the following symptoms following phrenicectomy: one of eructations of gas, another of "heart burn" a third of vomiting and two of dysphagia. One of the latter symptoms occurred after a right-sided phrenicectomy. Our observations were made on patients who had phrenicectomy performed for pulmonary tuberculosis (nineteen cases), bronchiectasis, chronic abscess of the lung, chronic empyema or hemoptysis.

We have considered our cases as follows:

1. Left-sided phrenicectomies with marked elevation of the paralyzed leaf of the diaphragm.

<sup>16</sup> Uebelhoei O. *Relaxatio diaphragmatica nach kunstliche Zwerchfellahmung*. Deutsche Ztschr. f. Chir. **211**: 266, 1928.

<sup>17</sup> Assmann H. *Klinische Röntgendiagnostik der inneren Erkrankungen*, ed. 4, Leipzig, F. C. W. Vogel, 1929.



- 2 Left-sided phrenicectomies with slight elevation of the paralyzed leaf
- 3 Left-sided phrenicectomies in cases in which there was a large left pneumothorax before, which was maintained following phrenicectomy
- 4 Right-sided phrenicectomies

We observed that the thoracic portion of the esophagus may be deflected to the right or the left because of fibrosis, pleural effusions, pneumothorax or kyphoscoliosis. The degree and acuteness of this deflection and whether or not it will be productive of symptoms are naturally dependent on the site and nature of the underlying lesion. Thus localized, mediastinal fibrosis with changes in the lung may affect

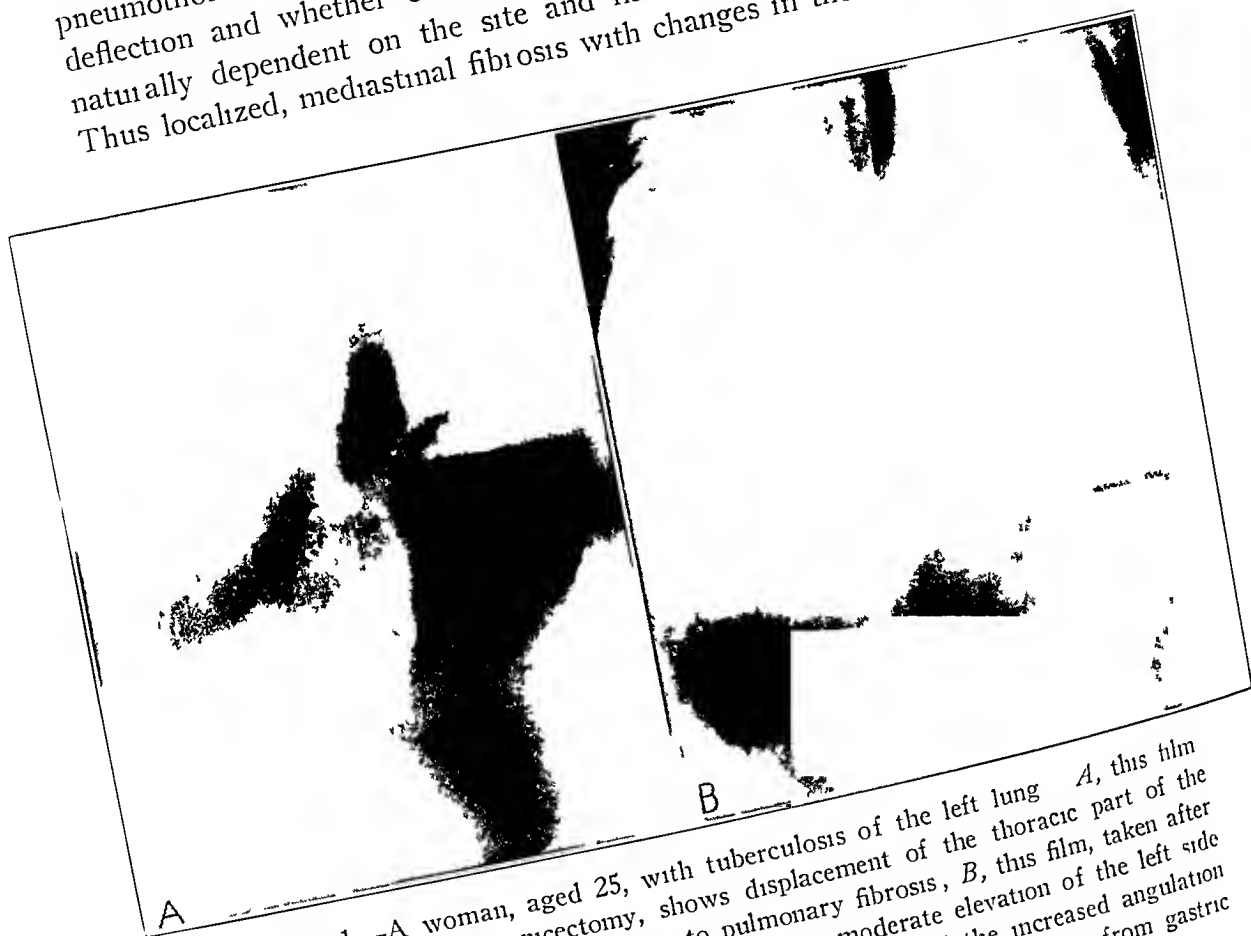


Fig 1—A woman, aged 25, with tuberculosis of the left lung. *A*, this film taken before the phrenicectomy, shows displacement of the thoracic part of the esophagus, the displacement is due to pulmonary fibrosis. *B*, this film, taken after the phrenicectomy had been performed, shows moderate elevation of the left side of the diaphragm. Note the large stomach bubble and the increased angulation of the abdominal portion of the esophagus. The patient was free from gastric symptoms.

the esophagus at only one point. In fact, as already mentioned, the esophagus was sometimes found permanently displaced to the affected side.

Concerning the upper half of the thoracic portion of the esophagus, we observed no marked mechanical displacement or shift with respiration following phrenicectomy.

Following phrenicectomy we did observe slight respiratory deflection of the lowermost thoracic portion of the esophagus. The normal contracting leaf of the diaphragm appeared to displace the lower part of the esophagus to the innervated side during inspiration, and permitted it to return to its former position during expiration.

Our chief interest was centered around the abdominal portion of the esophagus and what might happen to it following phrenicectomy. The abdominal portion of the esophagus could be affected in two ways: (1) as a direct consequence of the anatomic rearrangement following the rise in the diaphragm and (2) as a result of the pull of the opposite contracting diaphragm. Both could, of course, operate.

We have observed that elevation of the left side of the diaphragm following phrenicectomy results in upward displacement of the stomach and gives rise to a permanently large stomach bubble. We have noted that the curve that the esophagus normally makes after it leaves the hiatus to enter the stomach can become sharper (fig 1). Whether the upward displacement of the diaphragm and stomach is due to negative intrathoracic pressure, increased intra-abdominal (or intra-alimentary) pressure or disproportion between the two we do not know. The colon may also come to occupy a position within the thorax. One cannot with absolute certainty say that the stomach and colon follow the diaphragm in a purely passive way. Certainly interposition of other structures between the diaphragm and the stomach is rare.

Fluoroscopic examination of one patient following right-sided phrenicectomy showed that the barium-filled stomach became deflected to the right with each inspiratory contraction of the left side of the diaphragm.

Dr Sherwood Moore<sup>18</sup> observed that there may be displacement of the pylorus to the left in cases in which the fundus is displaced upward. He therefore suggested that this upward displacement might be due to contraclockwise rotation of the greater curvature, the lesser curvature remaining more or less fixed. This would tend to prevent marked distortion of the abdominal portion of the esophagus which would otherwise occur. He felt that this point requires further confirmation.

Our observations in the cases grouped in the manner previously noted have been as follows:

1. Cases that resulted in a marked elevation of the left diaphragm also showed a very large stomach bubble and increased angulation of the abdominal portion of the esophagus (fig 2). Such angulation following phrenicectomy is not of serious moment.

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18 Moore, Sherwood. Personal communication to the authors.

2 Those cases which resulted in only slight elevation of the left side of the diaphragm failed to show any marked change in the position of the abdominal part of the esophagus (figs 3 and 4)

3 Those cases in which there was a large left pneumothorax before and after phrenicectomy also showed only moderate elevation of the diaphragm and consequently little or no increased angulation of the abdominal part of the esophagus

4 We failed to observe any definite permanent change in the abdominal part of the esophagus following right-sided phrenicectomy

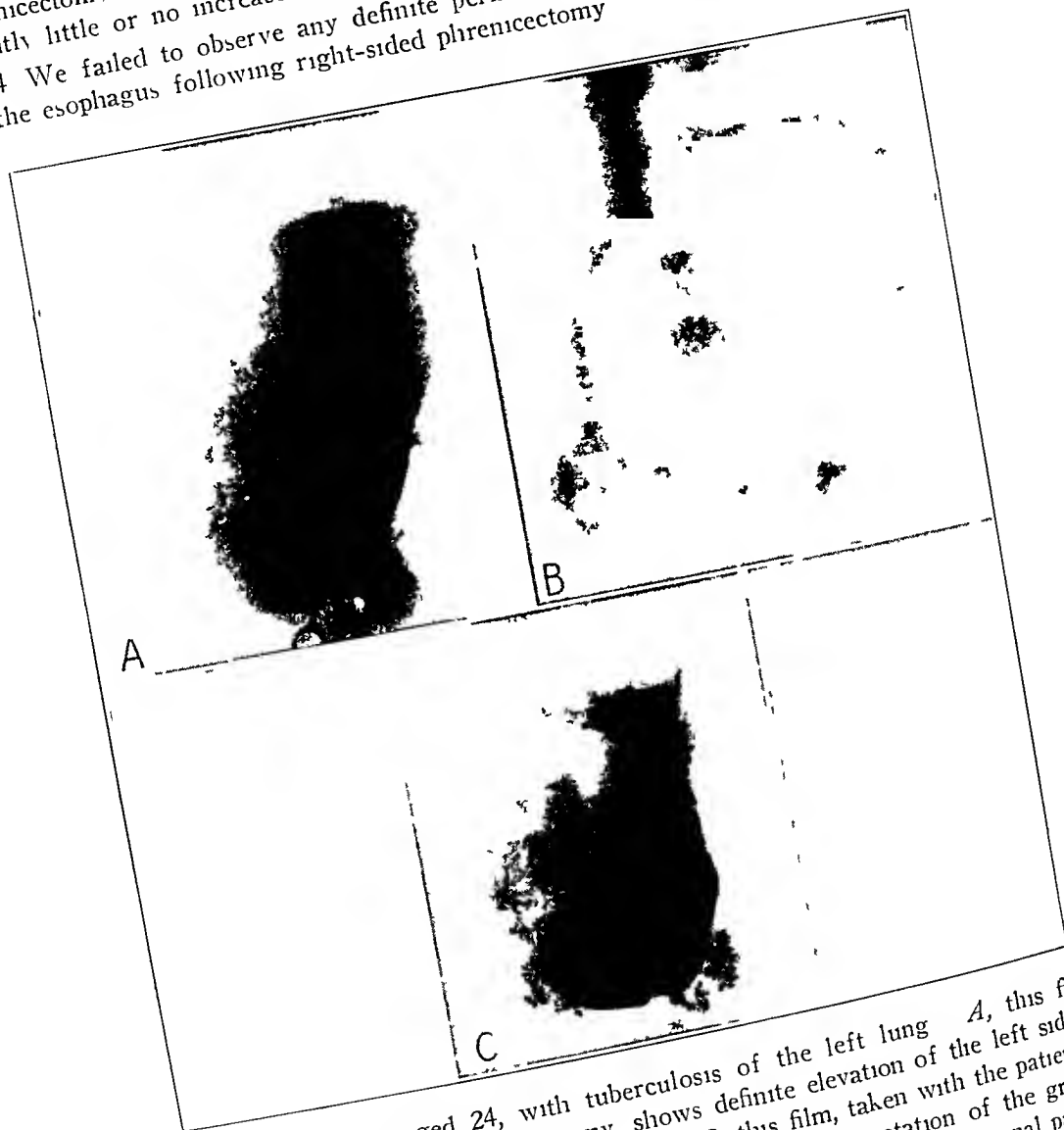


Fig 2—A man, aged 24, with tuberculosis of the left lung. *A*, this film taken ten months after phrenicectomy, shows definite elevation of the left side of the diaphragm and a large stomach bubble. *B*, this film, taken with the patient in the recumbent position strongly suggests contraclockwise rotation of the greater curvature of the stomach. *C*, note the marked angulation of the abdominal part of the esophagus. A complete series of roentgenograms of the gastro-intestinal tract showed increased alimentary motility chiefly of the colon but without localization in the cecal portion. The patient was troubled with vomiting.

When the barium mixture is thin there is no delay in the flow from the esophagus to the stomach either before or after phrenicectomy. When a thick paste is used, however, the bolus may be held up in the

esophagus and the normal "milking action" observed, that is, the barium enters the stomach during expiration. During inspiration the flow of barium seems to be interrupted, so that no barium is observed in the esophagus below the diaphragm. This milking action is not impaired following unilateral right-sided or left-sided phrenicectomy. We have not had an opportunity to study the "milking action" in a patient in whom both phrenic nerves were cut. From the experimental work done by Sauerbruch<sup>8</sup> we would expect the milking action to be lost in the case of bilateral phrenicectomy.



Fig. 3—A man, aged 26, a patient of Dr. Duff Allen, had tuberculosis of the left lung. A left-sided phrenicectomy was performed on Oct. 14, 1929. This film, taken in April, 1930, shows displacement of the thoracic portion of the esophagus which is due to pulmonary and mediastinal fibrosis. The left side of the diaphragm is only moderately elevated. There is a large stomach bubble, but only slight angulation of the abdominal part of the esophagus. The patient began to complain of eructations of gas, six months after the phrenicectomy.

We have failed to observe any marked delay in the emptying of the esophagus following phrenicectomy.

It is obvious that we have endeavored to draw some analogy between an eventrated diaphragm and a high paralyzed diaphragm following phrenicectomy. The etiologic factor may be the same in both, injury or destruction of the phrenic nerve. Histologically the diaphragm in both cases is atrophic. An anatomic rearrangement of the normal

relationship between stomach and esophagus exists in both. We believe that phrenicectomy has been performed so frequently without the production of symptoms that, as in the case of eventration of the diaphragm, perhaps some hitherto unmentioned factor is necessary to precipitate symptoms.

It is difficult to localize the symptoms noted by our patients in any one part of the gastro-intestinal tract. Air which normally collects in the stomach may fail to be expelled readily following phrenicectomy.



Fig. 4—A woman, aged 22, a patient of Dr. Duff Allen. A right-sided phrenicectomy was performed for pulmonary tuberculosis. This film shows displacement of the thoracic portion of the esophagus which is the result of pulmonary fibrosis. Fluoroscopic and roentgen examination failed to show any increase in the size of the stomach bubble and no increased angulation of the abdominal portion of the esophagus. The normal milking action of the diaphragm could still be observed after the diaphragm had been paralyzed.

because of the loss of the contractile power of the diaphragm. This in itself may be sufficient to produce symptoms.<sup>19</sup>

<sup>19</sup> Knosp, J. Die Therapie des gastrokardialen Symptom Komplexes. *Zt.-chr. Ärztliche Fortbildung* 15 720 (Nov.) 1929.

THE APPARENT OCCURRENCE OF "CARDIOSPASM" FOLLOWING  
PHRENICECTOMY

We observed so-called "dysphagia paradoxa" only in the 1  
in whom "cardiospasm" developed

REPORT OF CASE

CASE 1—A white woman, aged 36, was first admitted to Barnes Hos  
Oct 23, 1927, with complaints of cough associated with choking and vo  
expectoration and the loss of 20 pounds (9 Kg) in weight in two years T



Fig 5—A woman, aged 36, with bilateral bronchiecta  
phrenicectomy was performed on April 12, 1928 Two mon  
developed A, this film, made during October, 1929, shows  
the esophagus, above the diaphragm, and an even, smooth narr  
extremity of the esophagus, B, this film, made two days after  
examination, shows the bronchial tree outlined with iodized  
outlined with barium The left side of the diaphragm is sh  
is no marked angulation of the abdominal portion of the c

patient had had repeated attacks of pneumonia She had  
stipation and occasional pain in the left lower quadrant

Her present illness began when she was 6 years of age  
at that time, and from 1907 to 1926 she had recurrent  
lasted for a considerable period every winter Her

foul and rather copious. She also had fever, sweats and chills. Her attacks of coughing occasionally caused vomiting.

On admission her complaints were apparently as severe as they had ever been. Physical examination showed many râles at the base of the left lung. An injection of iodized poppy seed oil 40 per cent (by the aspiration method) demonstrated the presence of bronchiectasis of the lower lobes of the lungs. Examinations of the sputum were repeatedly negative for tubercle bacilli, and the Wassermann reaction was negative. Artificial pneumothorax was attempted, but air could be introduced only in small amounts because of adhesions, so that this treatment was soon discontinued. The patient made some improvement on postural drainage.

A left phrenicectomy was performed by Dr. Graham on April 12, 1928. The patient was discharged from the hospital ten days later. The left side of her diaphragm was paralyzed and definitely elevated.

One and one-half years after the phrenicectomy the patient was readmitted to Barnes Hospital (October, 1929). Her chief complaint was dysphagia. She stated that the difficulty in swallowing developed two months after phrenicectomy. At the time of admission dysphagia was less marked than it had been two months previously. Liquids caused more difficulty than solids, and she occasionally regurgitated undigested food. She also complained of substernal oppression. She had no pain and had not lost weight. A roentgenogram made shortly after admission showed an even dilatation of the esophagus (fig. 5). This dilatation seemed to start a short distance above the diaphragmatic opening of the esophagus. There was an even smooth narrowing of the lower extremity of the esophagus. Dr. Arbuckle made an esophagoscopy examination on Oct. 11, 1929. The patient received  $\frac{1}{6}$  grain (108 mg.) of morphine and  $\frac{1}{150}$  grain (0.4 mg.) of atropine thirty minutes before esophagoscopy was performed. No local anesthesia was used, and it is noteworthy that the patient did not gag or show any sign of feeling the tube. The esophagus was found to be filled with frothy mucus from a point just below the cricopharyngeus muscle down to the diaphragm. The mucosa of the esophagus appeared otherwise normal. At the level of the diaphragm the interior of the esophagus resembled an old-fashioned tobacco pouch closed by twisting. The right wall of the esophagus seemed to travel posteriorly, and the left wall anteriorly, in making the twist. The lumen of the esophagus at the level of the diaphragm could be readily dilated to admit the full-sized tube. The stomach appeared normal.

Following esophagoscopy the patient was given atropine sulphate,  $\frac{1}{200}$  grain (0.3 mg.), twice a day. Fluoroscopy four days later still showed a dilated esophagus, but the flow of barium into the stomach was more prompt, and the patient was symptomatically improved.

#### PHRENICECTOMY AND CARDIOSPASM

We are forced to comment on the relationship of the diaphragm to "cardiospasm," as we have noted one possible case following phrenicectomy.

Jackson stated that of hundreds of cases of so-called cardiospasm he had never seen any in which the spasm at the hiatus was any greater than what might be called maximum normal. His opinion, based on esophagoscopy observations, is that the failure to open, and not excessive spasm of the diaphragmatic pinchcock is the chief etiologic factor.

in many of the cases of cardiospasm Rieder<sup>20</sup> noted that the spasm which is felt by one's finger in the esophagus does not disappear if the vagi are cut It disappears, however, when both phrenic nerves are cut (Sauerbruch<sup>8</sup>) Rieder has never been able to produce cardiospasm experimentally

Sauerbruch<sup>8</sup> considered the sling of the diaphragm to be all-important in the production of "cardiospasm" Guns<sup>21</sup> pointed out that a phrenospasm may be found in normal subjects, and cardiospasm in patients with esophagectasia He stated further that at the beginning of an acquired dilatation of the esophagus, a phrenospasm exists It is later changed into a cardiospasm It is interesting to note that Birnberg<sup>22</sup> stated that both Douglas and Morrison blocked phrenic nerves of patients with alcohol in an effort to relieve cardiospasm, but without result Ernst<sup>23</sup> did not observe any obstruction at the cardia in forty-one patients following phrenicectomy

As symptoms of cardiospasm developed in one patient two months after phrenicectomy, and as we found definite evidence of the condition eighteen months later, it was suggested that cardiospasm might be a consequence of phrenicectomy

#### EXPERIMENTS ON ANIMALS

Our experimental investigations were carried out on dogs The following questions were considered

1 Is there any obstruction at the lower end of the esophagus following phrenicectomy?

2 Does an elevated diaphragm result in displacement of either the thoracic or the abdominal portion of the esophagus?

3 Does the esophagus become deflected by respiratory movements of the diaphragm on the nonparalyzed side following phrenicectomy?

4 Is the size or shape of the esophagus altered following phrenicectomy?

5 Is there any evidence of so-called "cardiospasm" following phrenicectomy?

*Technic*—All our experiments were performed on dogs In the early experiments the animals were given ether anesthesia It was soon noted that the esophagus appeared extremely dilated as a result Anesthesia was therefore not used when the roentgenograms were made Various means of filling the esophagus with an opaque meal were tried The best results were obtained by using an

20 Rieder, W Der sogenannten Cardiospasmus Eine experimentelle Studie Deutsche Ztschr f Chir **217** 334, 1929, Klinik und Therapie des sogenannten Cardiospasmus, *ibid* **222** 47, 1930

21 Guns P Phrenospasm and Cardiospasm in Mega-Esophagus, Arch Otolaryng **8** 156 (Aug) 1928

22 Birnberg T L Cardiospasm in the New-Born Infant Am J Dis Child **38** 1183 (Dec) 1929

23 Ernst M Kunstliche Zwerchfellahmung und Cardiospasmus Deutsche Ztschr f Chir **220** 258 (Nov) 1929



ordinary 50 cc syringe to inject the barium mixture through a rubber catheter, which was introduced into the esophagus through a perforated wooden mouth gag. The catheter was passed into the upper third of the esophagus, so that complete filling of the lower two-thirds was obtained. Roentgenograms were taken immediately following the injection.

The phrenic nerve was severed in the thorax close to the diaphragm. All phrenicectomies were performed under ether anesthesia. The positive pressure machine of Erlanger and Gessel was employed.

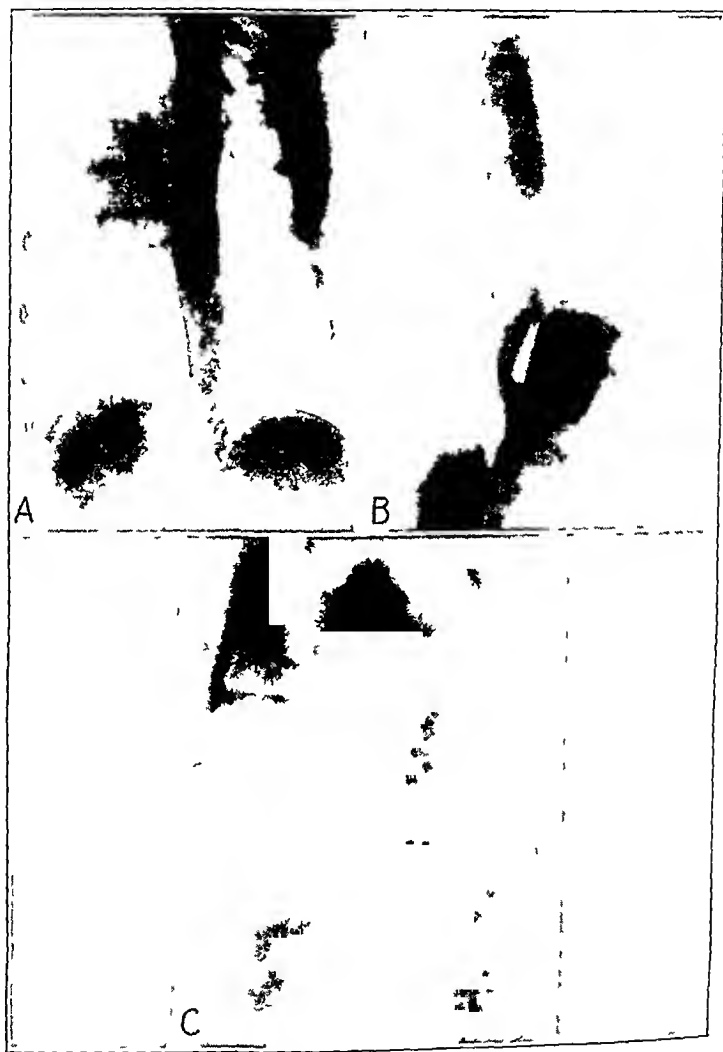


Fig 6—Dog 324. *A*, this film, taken in slightly oblique position shows a normal esophagus, *B*, this picture, taken after the phrenicectomy, shows definite elevation of the left side of the diaphragm and increased angulation of the abdominal portion of the esophagus, the fundus of the stomach lies high beneath the elevated left side of the diaphragm, *C*, in this film, taken seven weeks post-operatively, note the dilated esophagus. Barium has not been prevented from entering the stomach.

*Left Phrenicectomy.* Dog 324—Control films taken on Dec 10, 1929, showed a normal esophagus. The left phrenic nerve was cut on the following day. A film taken ten days after the operation showed the left side of the diaphragm

definitely elevated. There seemed to be increased angulation of the abdominal part of the esophagus. This resulted from the ascent of the fundus of the stomach beneath the elevated leaf of the diaphragm. This film was taken in a slightly oblique position so that the barium filled stomach would not overlap the abdominal portion of the esophagus. Definite dilatation of the esophagus was noted in a film taken seven weeks after operation (fig 6). The animal ate well and did not

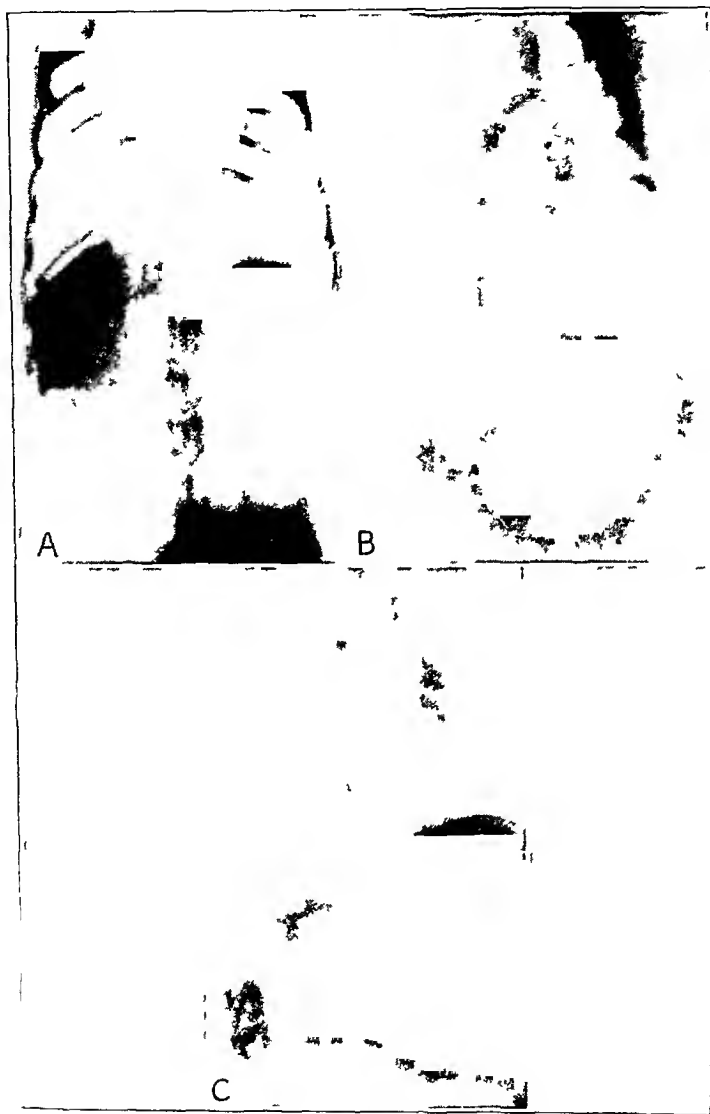


Fig 7—Dog B10. *A*, a control film, taken March 28, 1930, *B*, appearance following left-sided phrenicectomy which was performed on April 1, *C* this film, taken on the eighth postoperative day shows slight elevation of the left side of the diaphragm with but slight upward displacement of the stomach. Note the double shadow cast by the esophagus. This is due to the fact that both phases of respiration have been registered on the same film. It probably indicates the amount of esophageal displacement by the normal contracting right diaphragm.

lose weight. At no time was there any evidence of obstruction at the cardiac end of the esophagus. This dog was killed by other dogs on March 8 which was the seventy-seven day after operation. Necropsy showed that the trachea was

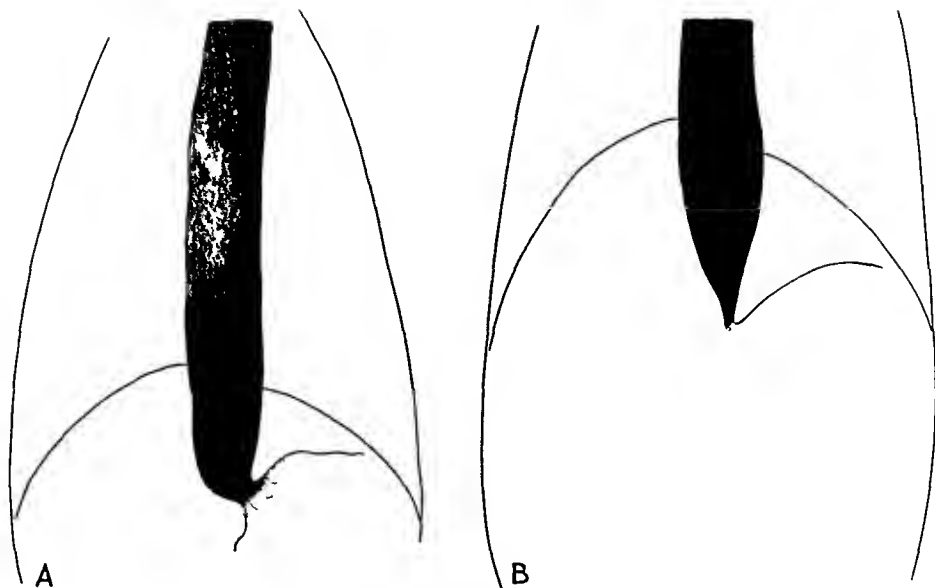


Fig 8—Dog 300 *A*, a control film taken on Dec 27, 1929, a right-sided phrenicectomy was performed on Jan 8, 1930, *B* this film, taken on the twelfth postoperative day, shows elevation of the right side of the diaphragm but no displacement of the abdominal portion of the esophagus or the stomach

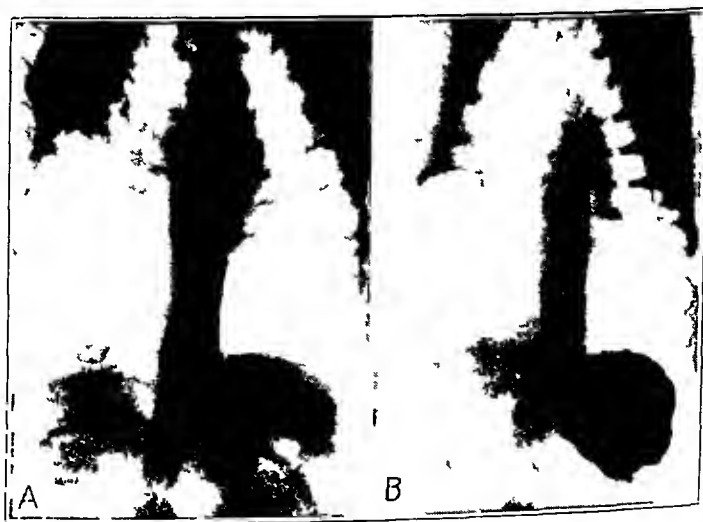


Fig 9—Dog 5441 *A*, normal esophagus, *B*, this film shows definite elevation of the right side of the diaphragm. The lower thoracic part of the esophagus is displaced to the left. Barium has entered the stomach. There is no evidence of increased angulation of the abdominal portion of the esophagus and no evidence of obstruction at the lower end of the esophagus

crushed. The left pleural cavity was clean. There were a few pleural adhesions between the lower lobe of the left lung and the muscularly atrophic elevated diaphragm.

Dog B 10—Control films, taken on March 28, 1930, showed what appeared to be a normal esophagus. A left-sided phrenicectomy was performed on April 1. A film taken on the eighth postoperative day showed slight elevation of the left

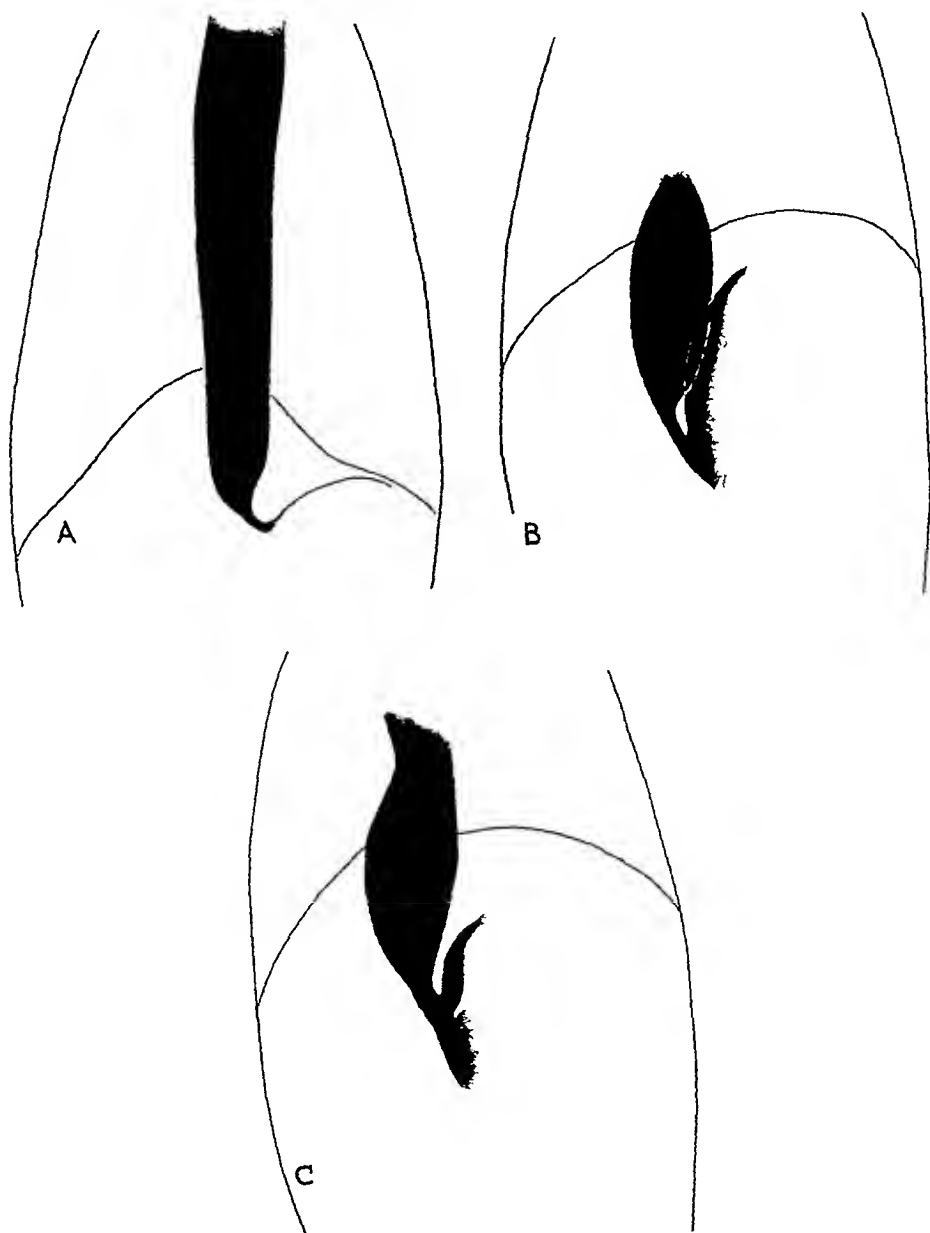


Fig 10—Dog 348. *A*, control film, made on Jan 8, 1930, *B*, a left-sided phrenicectomy was performed and the diaphragm plicated. This film was taken five days postoperatively. The stomach did not show the upward displacement noted following simple elevation of the left side of the diaphragm. There is no increased angulation of the abdominal portion of the esophagus. *C* this film, taken twelve days postoperatively, shows no evidence of obstruction at the lower end of the esophagus.

side of the diaphragm with slight displacement of the stomach. This was not sufficient to cause increased angulation of the abdominal portion of the esophagus. Another film taken on the same date during both phases of respiration showed a double shadow of the esophagus, which probably indicates the amount of esophageal displacement by the normally contracting right side of the diaphragm (fig 7). It should be noted that two films taken on the same date show a wider esophageal shadow in one than in the other. We believe that this was due to overfilling of the esophagus with barium.

*Right Phrenicectomy.* Dog 300—Control films were taken on Dec 27, 1929, and a right-sided phrenicectomy was performed in the manner already described. Films taken at intervals following operation showed elevation of the right side of the diaphragm, but we did not observe any change in the size, shape or position of either the thoracic or the abdominal part of the esophagus (fig 8).

Dog 5441—Control films were taken on April 1, 1930, and showed a normal esophagus. A right-sided phrenicectomy was performed on the same day. A roentgenogram taken on the eighth postoperative day showed definite elevation of the right side of the diaphragm. The lower thoracic part of the esophagus was displaced to the left, probably being pulled over by the normal contracting left leaf of the diaphragm. Some of the barium had entered the stomach. There was no evidence of obstruction at the lower end of the esophagus and no increased angulation of the abdominal portion of the esophagus, as had been noted in the case of a diaphragm the left side of which is high (fig 9).

*Left-Sided Phrenicectomy with Plication of the Left Side of the Diaphragm.* Dog 348—A control film showed a normal esophagus. On Feb 26, 1930, a left-sided phrenicectomy was performed, and the left leaf of the diaphragm was plicated by two purse-string sutures and one row of transverse sutures. Films taken on the fifth postoperative day showed an elevation of the left side of the diaphragm. The stomach failed to follow the rising diaphragm. This may have been due to actual increase in thickness of the diaphragm because of the plication or to unequal elevation of the diaphragm. The lower part of the esophagus was seen to be filled with barium, but no angulation of the abdominal portion of the esophagus was noted. Repeated films yielded similar observations (fig 10).

*Comment.*—Experiments on fourteen dogs gave further evidence of the close relationship between the esophagus and the diaphragm. They failed to show that paralysis of one part of the diaphragm seriously impairs the normal function of the esophagus. We did not observe any displacement of the thoracic or abdominal portion of the esophagus following phrenicectomy which was sufficient to offer roentgenologic evidence of obstruction. In dogs we have observed that the lower part of the thoracic portion of the esophagus may be pulled to the side of the normally contracting leaf of the diaphragm. This is in accordance with the observation made by Truesdale<sup>24</sup>. This deflection occurs during inspiration, but the esophagus returns toward the midline during expiration.

We did not make a fluoroscopic examination of our dogs to determine the effect of phrenicectomy on the milking action of the dia-

24 Truesdale P E. Congenital Hernia and Rupture of the Diaphragm. *Ann Surg* 90 654 (Oct) 1929.

phragm Our films nevertheless showed that the abdominal part of the esophagus is filled with barium during expiration and fails to fill during inspiration A thin barium mixture may outline this part of the esophagus during either phase of respiration

Whenever left-sided phrenicectomy was followed by a marked rise of the left side of the diaphragm we noted increased angulation of the abdominal portion of the esophagus This increased angulation however was never sufficient to produce evidence of obstruction or delay to the flow of barium from the esophagus to the stomach Increased angulation was not noted in any case of right-sided phrenicectomy

Two dogs seemed to show dilatation of the esophagus following phrenicectomy One of these dogs is still alive, and plates of the thoracic portion of its esophagus show an even dilatation throughout its entire length without any evidence of obstruction at the lower part We have noted that overfilling with a very thick mixture will result in such an apparent dilatation We feel confident that this is not the only factor producing dilatation of the esophagus in this animal It is interesting to note that the dog has become extremely emaciated He was operated on on Nov 2, 1929, six months before the present writing We therefore reserve judgment as to the possible late consequences of phrenicectomy in these dogs

The following are the answers to the questions that prompted our experimental investigation

- 1 There is no evidence at present that phrenicectomy results in obstruction at the lower end of a dog's esophagus
- 2 Marked elevation of the left side of the diaphragm may result in increased angulation of the abdominal portion of the esophagus
- 3 After unilateral phrenicectomy there is deflection of the lower thoracic part of the esophagus by the normally contracting leaf of the diaphragm
- 4 Evidence of slight dilatation of the esophagus has been noted several months after left-sided phrenicectomy
- 5 There is no evidence that phrenicectomy can produce cardiospasm in dogs

#### THE SO-CALLED GASTROCARDIAC COMPLEX

We noted cardiac symptoms on two occasions following phrenicectomy These symptoms were palpitation and dyspnea For this reason we had electrocardiograms made both before and after phrenicectomy Before reporting our experiences we shall present some general considerations

Mittenleiter,<sup>25</sup> among others, drew attention to the action of the diaphragm on the circulation This action may be indirect through

<sup>25</sup> Mittenleiter M Die Bedeutung des Zwerchfells für den Blutkreislauf, Deutsche Ztschr f Chir 188 379 1924

changes in respiration, the result of altered intrathoracic or abdominal pressure, or direct through action on the heart and blood vessels

The greater portion of the inferior vena cava is intra-abdominal. Mittenleiter<sup>25</sup> noted that where it pierces the tendinous portion of the diaphragm there are practically no muscle fibers in the inferior vena cava. As it passes through the diaphragm it becomes rich in elastic tissue and smooth muscle. Anatomically under normal conditions the inferior vena cava should not be compressed, as it pierces the tendinous portion of the diaphragm.

It is conceivable that a diaphragm with an elevated right side might compress the inferior vena cava if adhesions are present. The heart can actually be greatly displaced, rotated or pressed on by an "intra-thoracic" liver or stomach, as these organs may become intrathoracic structures following phrenicectomy.

It is appreciated that phrenicectomy may actually do good and may improve the circulation when there are adhesions between the pericardium and the diaphragm (Brauer and Fischer<sup>26</sup>).

It has been observed that the intra-abdominal pressure is greater with abdominal respiration than with thoracic respiration. Mittenleiter<sup>25</sup> expressed the belief that the rise in the diaphragm and the action of the diaphragm alone affect the intra-abdominal pressure but little. He is of the opinion, however, that unilateral phrenicectomy diminishes the sucking action exerted on the veins.

As we are to refer to the term "gastro-cardiac complex" (gastro-kardiale Komplex), it is perhaps best to state what this term implies. When Roemheld<sup>27</sup> described this symptom-complex, he spoke of it as a neurosis. Patients so affected apparently have a neuropathic constitution and a heart that readily responds to stimuli. To this nervous basis is added a dyspeptic diathesis because of an accumulation of gas in the stomach. The symptom-complex thus calls for the following underlying conditions: a heart that readily responds to stimuli and is mobile (or mobile) and a chronic air bubble in the stomach.

#### PHRENICECTOMY AS A CAUSE OF THE GASTROCARDIAC COMPLEX

In discussing phrenicectomy as a cause of the so-called "gastro-kardiale Komplex," Hecht<sup>13</sup> pointed out that the dextrocardia that may result need not per se cause dyspnea. He reported, however, the occurrence of palpitation and extrasystoles in two instances. These

26 Brauer, L., and Fischer, H. Die Herzchirurgie unter Berücksichtigung physiologischen Fragestellungen, *Handb. d. norm. u. path. Physiol.* **7** 1877, 1927.

27 Roemheld, L. Der gastrokardiale Symptomkomplex eine besondere Form sogenannter Herzneurose, *Ztschr. f. phys. u. diätet. Therap.* **16** 339 1912.

extrasystoles could have been due to the dyspnea of excitation. Hecht<sup>17</sup> stated further that as long as the musculature of the heart is unimpaired and the circulation intact, phrenicectomy with resultant displacement of the heart should not produce any symptoms. Roemheld<sup>27</sup> would have us believe that a heart already displaced or rotated can be appreciably affected by a diaphragm elevated by an accumulation of gas in the stomach or by loops of distended colon beneath it.

Welles<sup>15</sup> noted that in a small number of his patients there developed a persistent tachycardia and a rise in pulse rate from 10 to 20 beats per minute following phrenicectomy.

Bernuth<sup>28</sup> reported the occurrence of a gastrokardiac complex following left-sided phrenicectomy for bronchiectasis in a girl, aged 12. The operation was performed in June, 1927. The diaphragm rose 2 cm. In November the child complained of palpitation and was cyanotic. The pulse rate was 180 per minute. There were extrasystoles. The electrocardiogram was indefinite. The patient's symptoms were relieved when she was placed on frequent small meals.

Berg<sup>29</sup> pointed out that the gastrokardiac complex can be associated with organic disease such as gastric ulcer and cholelithiasis.

#### THE ELECTROCARDIOGRAM AFTER PHRENICECTOMY

We sought to determine from the electrocardiogram whether a rise in the diaphragm following phrenicectomy produces a recognizable change in it. Ten patients had electrocardiograms made before and after phrenicectomy. Nine had electrocardiograms made only after phrenicectomy. In no instance was the presence of organic heart disease demonstrated before phrenicectomy. We are therefore unable to say what effect phrenicectomy would have on an already diseased heart. As already noted, only two patients complained of palpitation and dyspnea. In one instance in which paroxysmal tachycardia was clinically suggested after phrenicectomy the electrocardiogram was normal.

Dr Julius Jensen of the department of cardiology carefully studied the records of those patients who had the electrocardiogram made before and after phrenicectomy. His report reads:

The records showed no marked changes. Four records showed no changes whatever and two records showed changes which were not conclusive. In one of these there was inversion of the T waves in lead III. Four showed definite changes in the heights of the complexes but not in their shape.

28 Bernuth, F. V. Gastrokardialen Symptomkomplex nach Phrenicusexercise bei einem zwölfjährigen Kinde, *Beitr. z. Klin. d. Tuberk.* **71**: 256, 1922.

29 Berg, H. H. Zur Klinik der Gastrokardialen Beschwerde. *Ztschr. f. klin. Med.* **108**: 186, 1928.



The following cases illustrate some of the changes noted

CASE 2—A girl, aged 18, had abscess of the lung. The mediastinum was not fixed. Right-sided phrenicectomy resulted in a slight rise in the diaphragm. Dr. Jensen reported the following changes: "A left axis deviation with upright T waves in lead III changed to a normal electrocardiogram with inverted T waves in lead III. This effected a lowering of T waves in lead II."

CASE 3—A woman, aged 20, had bilateral bronchiectasis and a fixed mediastinum. The diaphragm became slightly elevated following a right-sided phrenicectomy. An electrocardiogram showed that the complexes in lead III were heightened and that the T waves of the same lead were lowered after phrenicectomy.

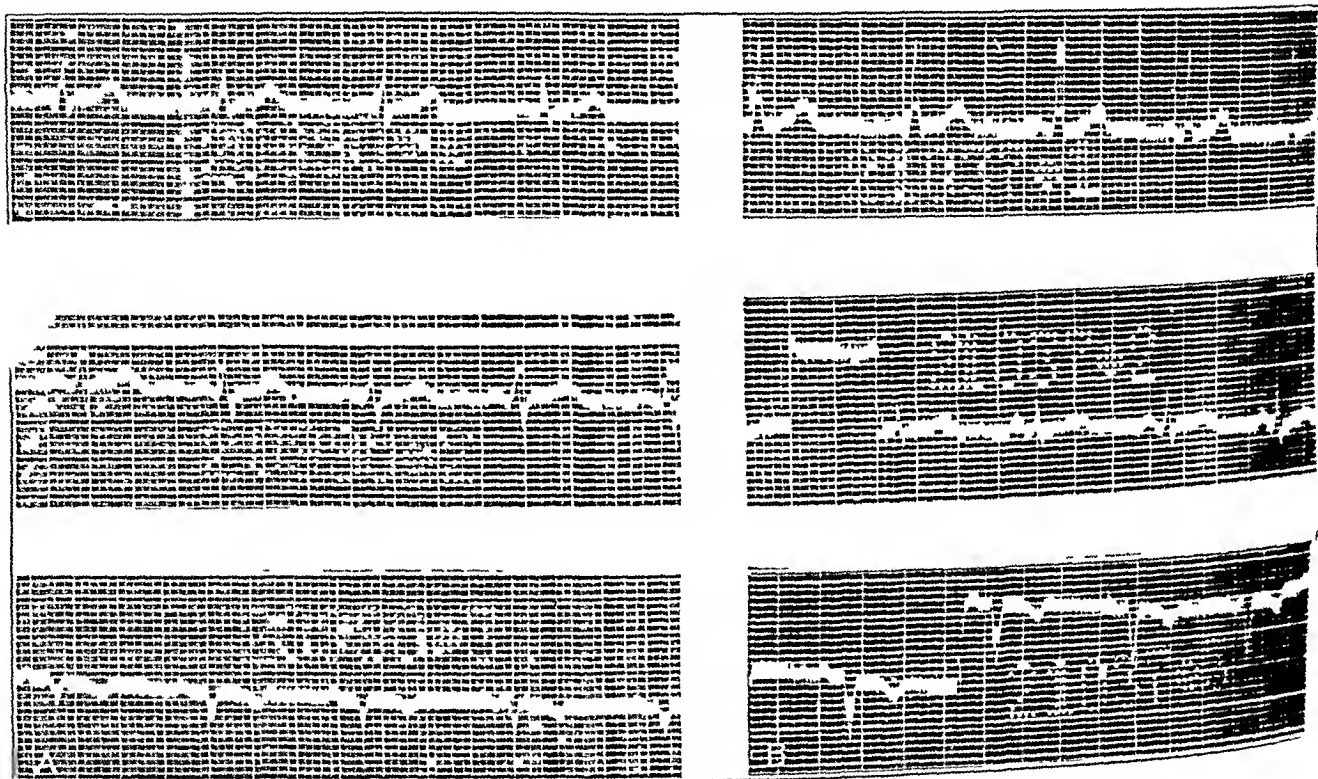


Fig 11—Electrocardiograms taken before (a) and after (b) phrenicectomy in case 3

CASE 4—A man, aged 38, had had chronic abscess of the lung and bronchiectasis on the left side. This patient had been treated previously by Dr. Graham by cauterly pneumectomy, following which he was well except for an anatomic defect and bronchial fistula. Phrenicectomy was performed as a preliminary step in closing the bronchial fistula. Left-sided phrenicectomy resulted in a high closing the diaphragm and displacement of the heart with apparent rotation of it. The cardio-phrenic angle became more acute as a result of displacement of the apex upward. The electrocardiogram showed that the QRS complexes in lead I became higher, and those in lead III deeper, following phrenicectomy (fig 11).

This patient was later subjected to a complete thoracoplasty and a successful plastic operation following phrenicectomy. Cardiac symptoms did not develop after these operations.

CASE 5—A man, aged 25, had pulmonary tuberculosis and cavitation on the left side. This patient received pneumothorax treatment before and after phrenicectomy.

tomv We believe that elevation of the diaphragm following phrenicectomy was somewhat inhibited by the presence of a large pneumothorax pocket. The mediastinum was not fixed, and there was displacement of the heart into the right side of the thorax. This displacement probably occurred as a result of the phrenicectomy, since the amount of air introduced at refills was the same before and after operation. The electrocardiogram showed that the low or almost inverted QRS complexes in lead III became definitely upright.

Electrocardiograms of nine patients of whose heart action only tracings were made after the operation were considered normal.

The slight changes in the complexes were interpreted as being due to changes in the cardiac axis caused by the altered position of the heart.

#### SUMMARY

Phrenicectomy may be followed by gastro-intestinal symptoms. Twenty-seven patients were examined before and after phrenicectomy. These patients were given a barium meal and underwent fluoroscopic examination, in many instances roentgenograms were taken before and after phrenicectomy. The phrenicectomies were performed for pulmonary disease. Five patients complained of the following symptoms after phrenicectomy: one of eructations of gas, another of heart burn, a third of vomiting and two of dysphagia. In all but one instance these complaints were temporary. With but one exception, they followed left-sided phrenicectomy. A case of cardio-spasm which apparently followed phrenicectomy is recorded.

No marked mechanical displacement or shift of the upper third of the intrathoracic portion of the esophagus was noted after phrenicectomy. Slight respiratory deflection of the lowermost intrathoracic portion of the esophagus was noted. The normally contracting leaf of the diaphragm appears to displace the lower part of the esophagus to its side during inspiration, but permits the esophagus to return to its former position during expiration.

The curve that the esophagus normally makes after it leaves the pillars of the diaphragm to enter the stomach can become sharper following left-sided phrenicectomy. In no case observed was this of serious moment. It is suggested (Moore) that the upward displacement of the stomach might be due to rotation of the greater curvature. Cases that have resulted in only slight elevation of the left leaf of the diaphragm have failed to show any marked change in the position of the abdominal portion of the esophagus. Patients with a large left pneumothorax before and after phrenicectomy showed only moderate elevation of the diaphragm after phrenicectomy and little or no increased angulation of the abdominal portion of the esophagus. We failed to observe permanent change in this part of the esophagus fol-

lowing phrenicectomy. We did observe respiratory deflection of the stomach after right-sided phrenicectomy.

The normal milking action could still be observed following phrenicectomy. We have no absolute proof that phrenicectomy per se may cause obstruction at the lower end of the esophagus.

Experimental studies on dogs yielded data similar to the clinical observations, but gave no evidence of esophageal obstruction following phrenicectomy.

The electrocardiogram showed no marked changes following phrenicectomy. Four patients showed changes in the height of the complexes but not in their shape. Two followed left-sided, and two followed right-sided phrenicectomy.

#### CONCLUSIONS

1 Gastro-intestinal symptoms of a transient character are not infrequent following unilateral phrenicectomy. They are of no serious consequence.

2 Deflections of the lower thoracic part of the esophagus occur following unilateral phrenicectomy and result from inspiratory contraction of the innervated leaf.

3 Permanent large stomach bubbles and increased angulation of the abdominal portion of the esophagus may occur following marked elevation of the paralyzed left leaf of the diaphragm.

4 The normal milking action of the diaphragm on the esophagus is not impaired by unilateral phrenicectomy.

5 There is no experimental evidence that phrenicectomy results in obstruction of the lower part of the esophagus or proof that phrenicectomy may produce "cardiospasm."

6 The electrocardiograms following phrenicectomy show no marked change.

#### ABSTRACT OF DISCUSSION

DR F. T. LORD, Boston. As I remember the cases of eventration of the diaphragm reported in the literature, there are symptoms of circulatory or gastro-intestinal disturbance in about one half of them. This anomaly, when discovered, may be assumed to have been of long duration, and it is a question whether these observations on rather recent cases of phrenicectomy can be regarded as an assurance that symptoms will not later develop. How long after the operation were these cases observed?

DR HARRY C. BALLON, St. Louis. Some of these patients were observed as long as three and one-half years after phrenicectomy. We do not know at the present time what the late consequences of phrenicectomy will be. It is well known that patients suffering from eventration of the diaphragm go for many years before any sign or symptoms develop. It is therefore possible that in some patients on whom phrenicectomy has been performed, other hitherto unmentioned late consequences may develop after ten or twenty days.

# IDIOPATHIC DILATATION OF THE ESOPHAGUS

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The disease variously known as idiopathic dilatation of the esophagus, cardiospasm or achalasia cardia has not rarely been diagnosed since the advent of the x-rays and the opaque meal, by those interested it is generally held to be second only to cancer in frequency of diseases of the esophagus.

The main interest in the study of a disease depends on new evidence of its causation if that has been in doubt, or new methods of treatment, if those used in the past have been unsatisfactory.

Of the many names offered, the one chosen, "idiopathic dilatation of the esophagus" suggests a confession of ignorance as to the cause, and a brief review of the methods of treatment shows wide divergence in principle.

Recent work by a group in Japan seems to offer a more definite and satisfactory explanation of the pathologic process. I hope to indicate a method of surgical treatment which, if not entirely new, has been only half-heartedly stated and not correlated to the pathologic process, yet which I believe is based on a true understanding of the mechanics of the disease, and which, easy and safe of accomplishment, has been successful in one instance.

It is probable that there has been included within this group more than one series of pathologic changes. These must be distinguished and separately classified. By this, I mean that true cardiospasm may be an entity, but a different disease than idiopathic dilatation.

I have recently had the opportunity to see in a new-born infant a condition that may well be looked on as cardiospasm comparable to infantile pyloric stenosis. Because the infant was vomiting, roentgen examination was made. The fluoroscopic examination showed the esophagus to be a little wider than was expected. The fluid food hesitated at the level of the diaphragm for some moments, there was then a series of strong peristaltic movements in the esophagus, the cardia opened and the food entered the cardiac end of the stomach. It was immediately and forcibly regurgitated. This was obviously something different from idiopathic dilatation.

Idiopathic dilatation signifies a diffuse enlargement of the lumen of the esophagus in which no mechanical obstruction exists. The dilatation is mostly in the lower two-thirds that is to say in the thoracic portion of the organ. The abdominal portion, the portion from  $1\frac{1}{2}$  to 2 inches (3.7 to 5 cm) below the diaphragm, is not dilated.

The esophagus is not only dilated, but also elongated. It may measure up to 46 cm. It must therefore become curved, so that frequently a large fold rests on the upper surface of the diaphragm. Often it may contain from 1,500 to 2,000 cc of fluid. The wall becomes thickened, the thickening being represented mostly in increase of the circular muscle fibers. The diameter may measure from 6 to 7 cm to 16 cm and the circumference 30 cm.

The mucosa may be normal, but more frequently it is inflamed. The tissue is then friable from inflammatory exudates.

The subdiaphragmatic portion requires special mention. It is never dilated. It is often described as normal, and the phrase keeps repeating itself, "thickened and contracted like a lead pencil."

On the three patients on whom I have operated, the subdiaphragmatic esophagus was a small, round, rather firm structure little larger than a pencil. It was not thickened and showed no sign of hypertrophy of the muscle. It measured about 1 cm in diameter and was round, as compared to the 1 inch (2.5 cm) diameter and flattened appearance of the normal structure.

Bull, in a publication in 1925, gave details of this portion of the esophagus as found at operation or post mortem in 104 cases. In 52 it was reported normal, in 52 altered. Thirty of these 52 were described as small, contracted pencil-like or less than 1 cm in diameter. Only 3 were described as hypertrophied.

It seems clear, therefore, that the cardia is found to be either normal or small, but not thickened.

The only significant microscopic observations are those of Kiouss and Ridder, who reported finding atrophy of the vagus nerve in one instance, and those of Rakes who found what he believed to be atrophy of Auerbach's plexus in three instances.

Bull reported that in 82 of 141 patients symptoms following the ingestion of food appeared before the age of 40.

The most important observations in a macroscopic study of the pathologic changes in the disease are that the dilatation occurs in the thoracic portion of the organ and ceases abruptly at the level of the diaphragm. Below this point, in the great majority of instances, it is a round cordlike structure which shows no increase in thickness of the muscular wall.

The esophagus is also lengthened, and may be folded over the surface of the diaphragm. The mucosa may be very friable or ulcerated, a point to be seriously considered in any form of manipulation.

Starting from this point, a group of Japanese investigators headed by Tamiya, have published a series of experimental studies which have gone far to explain the occurrence of the disease. From experiments

on the reaction to drugs of isolated strips of esophagus taken from the subdiaphragmatic portion, the details of which it is not necessary to elaborate, Tamiya concluded that the subphrenic part of the esophagus is supplied by both vagus and sympathetic fibers, and that the sympathetic fibers are mostly depressors.

The second step consisted of fluoroscopic studies on the esophagus of dogs after one-sided section of the vagus, the sympathetic and the vago-sympathetic trunk. This resulted in a marked delay in the passage of the food at the lower end of the esophagus. A pendulum movement developed, but the food did not pass on. This cannot be regarded as spasm, because there was never any resistance to the passage of bougies. The delay could also be overcome by filling the esophagus with fluid. A spastic closure does not occur, but there is failure to open, an achalasia. The closure of the cardia is then due to the normal autonomic tone.

The stoppage of food after the one-sided section was never permanent, and did not occur after a variable time, from days to weeks. It was not accompanied by dilatation. The result of the cutting of both vagi was a total loss of peristaltic action, a widening of the lumen and a stoppage of food at the level of the diaphragm.

The widening of the esophagus resembles that found in idiopathic dilatation. The cardia is closed from then till death, but not during a spasm. There is no resistance to the passage of bougies. Resistance can be overcome by filling the esophagus with water, which, when acting directly by its weight, opens the cardia.

An effort was then made to produce the same results by causing a degeneration of the nerves by painting with arsenic. Immediately after the treatment by arsenic, the food passed normally, but within twenty-four hours, concurrently with the appearance of sympathetic paralysis in the eye (myosis, ptosis and bulbar retraction), there was interference with the passage of food more or less similar to that occurring after cutting, and depending on the degree of degeneration of the vagi.

These experiments give strong support to the theory of Kious' that the disease is secondary to degenerative changes in the vagi, and that the closure is due to the normal tone acting without nerve control. The clinical picture is fairly constant. For the diagnosis two things are of great importance, the history of the onset and progress of the disease and roentgen examination.

The history of the condition usually begins before the patient is 40 years of age, and extends over years. There is mainly difficulty in swallowing food. Sometimes the onset is sudden, but progress is intermittent. As the disease progresses, regurgitation of large quantities of food becomes a feature. This food is frothy and mixed with saliva. The regurgitation of large quantities of food is in marked contrast to

the dysphagia of mechanical obstruction for in the latter the esophagus never contains the 1,500 to 2,000 cc common in idiopathic dilatation

The patient nearly always has learned certain tricks or contortions to aid the passage of food, and these have two common purposes to straighten out the elongated and crumpled esophagus and to add weight to the column of fluid. Thus these patients may stand up, raise the chin and stretch the neck like a chicken drinking and following the ingestion of food they may drink glass after glass of water. Some have been reported to be able to judge when the food has passed and then reject the water.

There is no more than the normal resistance to the passage of a bougie or stomach tube, and most persons have been fed by this means at times or constantly.

The long effort, the regurgitation and the contortions are most distressing to the patients and usually to those who have to eat in their presence.

The roentgen appearance is also characteristic. In no other disease is there seen the wide shadow associated with this condition. The shadow ends at the level of the diaphragm as a smooth rather bluntly pointed cone without the length of constriction or the irregularities of outline found in carcinoma.

The histories of the three cases here reported are illustrative of the disease.

#### REPORT OF CASES

CASE 1—Miss D, aged 50, was admitted to the hospital on Nov 1, 1926, complaining of difficulty in swallowing food. She first noticed this difficulty more than ten years before. After eating, she had pain at the lower end of the sternum. Her discomfort gradually increased, until during the past year she had great difficulty in getting enough food to keep her alive. She had lost about 50 pounds (22.7 Kg) and weighed 87 pounds (39.5 Kg). She took from two to three hours to eat a meal, using large quantities of water between mouthfuls. She twisted her head backward and to one side, held her breath and forced the food down. Often this resulted in regurgitation of most of the food taken. She ate alone. At times she was fed by tube. Dilatation by bougies and dilatation of the bag was tried, with only temporary relief. She urged that something be done.

Roentgen examination showed marked dilatation of the esophagus. Semisolid food remained in this organ, but fluid passed into the stomach, leaving a column about 3 inches (7.6 cm) high in the lower end of the esophagus. The shadow ended bluntly at the level of the diaphragm.

Extramucosal esophagoplasty was performed on Nov 15, 1926, Marwedel's incision being used. The subdiaphragmatic portion of the esophagus was less than half an inch (1.27 cm) in diameter. The muscle wall was not thickened but felt like a muscular cord. Immediately above the diaphragm, the esophagus was  $1\frac{1}{2}$  inches (3.7 cm) in diameter. The dilated portion was brought through the diaphragm, and the muscle incised down to the submucosa well on to the

cardiac end of the stomach. The wound was closed without drainage. From the time of operation to the present day she has taken food freely. She gained 30 pounds (13.6 Kg) in weight, eats her meals with the rest of the family, and is living a normal life.

Roentgen examination somewhat over a year after operation showed that the esophagus filled with food 6 inches (15.2 cm) above the diaphragm before any passed into the stomach, then the whole mass passed on rapidly.

CASE 2—J. P., aged 35, was admitted to the hospital on Feb. 27, 1928. The condition began about nine months before admission, the onset being characterized by sudden acute pain and regurgitation of food. The regurgitated material contained undigested food, water and saliva. The food was returned about five minutes after ingestion following a sensation of the food sticking at the lower end of the sternum. The patient's appetite was good, and she complained constantly of hunger. The symptoms became persistent and severe. She lost 49 pounds (22.2 Kg) and felt dizzy and weak from lack of food.

Atropine was tried without benefit. Feeding by tube was instituted. The tube passed easily. Roentgen examination showed a six hour retention of food at the cardiac end of the esophagus, a column of barium 6 inches long and an empty stomach.

On February 28, a Heller extramural esophagoplasty was attempted on the strength of the success in the previous case. The subdiaphragmatic portion of the esophagus was found to be three-fourth inch (1.9 cm) in diameter. The wall was thin. The muscular wall over the cardiac end of the stomach was incised down to the submucosa, and the cut was extended up onto the esophagus. The procedure seemed satisfactory up to this point, when, without obvious reason, a small leak was observed. This quickly enlarged to a hole one-fourth inch (0.63 cm) in diameter as the mucosa was either ulcerated or very soft. The opening was sutured and reinforced by peritoneum, a pad of omentum was sewn over this, and the wound was closed with a drain to the line of suture.

The patient died on the sixth day from an obvious mediastinal infection.

Autopsy showed a longitudinal opening in the esophagus 6 cm above the sutured incision. Microscopic section showed a thin necrotic margin. There was no change in Auerbach's plexus similar to that described by Rakes in *Guy's Hospital Reports* of 1920.

There have been advocated a variety of methods of treatment. It is not my intention to discuss these in detail. It is natural that the simpler methods should be tried first and that operation should not be urged in the less severe cases, but according to my understanding of the disease, these will be found ineffective and not without danger in the more severe types of the condition.

The methods of treatment have followed in general two main plans. The first methods include dilatation of the narrowed portion of the esophagus either from the inside by bougies or by dilatable bags or dilatation by the finger introduced through an opening through the stomach.

If the pathologic process as described by Taniguchi is correct, neither of these methods can be considered either sound in principle or without



the danger of tearing the narrow, relatively thin-walled, friable subdiaphragmatic portion of the esophagus

The second main line of treatment followed was the formation of an opening by suture between the dilated portion of the esophagus and the stomach. The objection to this is its danger, for though it has been successfully done a number of times, suture of the esophagus is notably unsatisfactory. Especially is this true in the inflamed state, when the tissues are sometimes so friable as to make suture most precarious.

The third method is that adopted successfully in the first of the three patients whose cases are reported here. Encouraged by the success in the first case, I attempted the same method in the second case, only to find tissue so friable or ulcerated that the mucosa was either absent or torn into the lumen, the sutures sloughed out, resulting in a fatal infection of the mediastinum.

In the third case the various surgical procedures were reviewed.

The first consideration was that in the most commonly adopted surgical methods one step was common to all. At one stage of the operation, the opening through the diaphragm was enlarged and the dilated portion of the esophagus brought down through the opening and held there by sutures.

The second consideration was suggested by the fluoroscopic examination of the first patient after the extramucosal esophagoplasty. Here the first view suggested that nothing had been accomplished, but when the column of fluid in the esophagus had reached a height of about 6 inches the resistance of the narrow subdiaphragmatic portion was overcome, just as it was overcome in Tamiya's experiments, and the food passed freely into the stomach. This was in marked contrast to the appearance before the operation, when the whole esophagus could be filled and remain full for long periods or until regurgitated. What was the difference? It seemed reasonable to suppose that when the dilated portion ended at the diaphragm, over-filling of the esophagus merely resulted in a still more marked kink just above the diaphragm, while after the opening of the diaphragm was enlarged and a part of the dilated portion brought through, the weight of the column of fluid could then act to a mechanical advantage and overcome the normal tonic resistance of the narrowed portion of the esophagus leading into the cardia.

In retrospect, it seemed unlikely that the extramucosal esophagoplasty in the absence of any thickening or hypertrophy of the muscles could be considered comparable to the Fredet-Ramsted pyloroplasty so successful in infantile pyloric stenosis. Moreover, the tissue conditions found in the second case, with the consequent wounding of the mucosa

and the sloughing of the infected wall had demonstrated that extra-mucosal esophagoplasty was dangerous besides being unnecessary

In the third patient, it was therefore deliberately planned that the operation should consist merely in the earlier steps *i. e.*, the exposure of the cardiac end of the stomach through the Maiwedel incision, the cutting of the coronary ligament of the liver and the turning downward and to the right of the left lobe of the liver. By this means the cardiac end of the stomach and the subdiaphragmatic portion of the esophagus are brought into view. Under the eye an incision was then to be made forward through the crura of the diaphragm. The dilated portion of the esophagus was brought through this opening for an inch or more. The main opposition is found in the vagi which may be cut with impunity more especially if Tanaya is correct in stating that they are already degenerated.

CASE 3—Mrs. B. M., aged 58, was admitted to the hospital on May 20, 1929. She had previously been admitted to the otolaryngologic department under Dr. Birkett in 1926. At that time she complained of difficulty in swallowing of one year's duration. The difficulty was more apparent with solid food than with fluid. She then had the sensation of "filling up" inside. If she tried to swallow after this she had to force the food down by violent efforts, often regurgitating through the nose. After a short rest, she forced another mouthful of food down.

In October, 1926, she was examined with the aid of the esophagoscope, and the cardiac end of the stomach was found markedly contracted and compressed about a large bougie, which could be easily passed. Roentgen examination demonstrated obstruction of the characteristic kind at the end of the diaphragm.

The patient was admitted to the surgical wards three years later in May, 1929.

The subsequent history showed gradually increasing difficulty in swallowing with frequent regurgitation of food. During the winter of 1928-1929, she had to be fed by tube during an acute illness. Since that time she had learned to pass the tube herself, and all nourishment was taken by this means. She lost 80 pounds (36.3 Kg.) during the three years.

On May 29, 1929, she was operated on, the same approach being used as in the other case, and the subdiaphragmatic portion of the esophagus was exposed. The opening between the crura of the diaphragm was enlarged by cutting forward until it admitted two fingers easily. The esophagus was then freed by blunt dissection and pulled down till  $1\frac{1}{2}$  inches of the dilated portion was brought through. To allow of this, the vagi were cut. The subdiaphragmatic portion of the esophagus was a small, round, cordlike structure about  $1\frac{1}{2}$  inches long and not more than  $\frac{1}{3}$  inch (0.7 cm.) in diameter. There was no hypertrophy of the circular muscle coat. Immediately above the diaphragm, the esophagus was  $1\frac{1}{2}$  inches in diameter, but not notably hypertrophied. The wound was closed without drainage.

The patient's recovery was smooth, and she has been able to swallow soft and liquid food in ordinary time. She sometimes has a sensation of fulness for from ten to fifteen minutes, which might suggest that food remained a time in the lower end of the esophagus. She has gained weight and strength.

By the operative procedure used here the grave danger of tearing the esophagus is avoided as the dangerous suture is not necessary.

Since the peristaltic movements of the esophagus are no longer operative in any case, the onward passage of food must depend on the pressure exerted by the column of fluid in the esophagus. The recognition of this mechanical factor seems to be essential to success in any operation. This procedure recognizes this factor, further, it is simple to carry out and should be free from the accident that is constantly to be feared in every other mechanical treatment—the tearing of the friable, inflamed esophagus.

On theoretical grounds, there should be no tendency to recurrence, for any cicatrix at the opening of the diaphragm would tend to widen, not to contract, the new opening.

The success attending the operation on the last patient is encouraging. Food can now be taken in good quantity and in ordinary time, the only precaution is that the food must be well divided and mixed with a fair quantity of fluid.

#### ABSTRACT OF DISCUSSION

DR A. T. BAZIN, Montreal, Canada. As Dr. Scrimger says, it is unfortunate that we cannot decide on the terminology. To my mind, "idiopathic dilatation" is an unsatisfactory term to describe this condition, unless there are a few cases that are associated with no causative lesion whatsoever. Many terms have been given to this disease, or subdivision of this disease if there are such, e. g., achalasia, an inability to relax. I do not see why we cannot be satisfied with "cardiospasm," provided we understand the anatomy and appreciate that it is not spasm of an orifice that we are dealing with, but spasm of a sphincter, and that the cardiac sphincter of the esophagus is at the level of the diaphragm. Moreover, it is easily pushed up above the level of the diaphragm.

I have had a limited experience with this malady. In fact, it seems to be difficult to educate the internists in the idea that cardiospasm is not purely a neurosis, they therefore hold these cases for an indefinite length of time. I have had three cases in the past two years, one of these, observed recently, was in a man, 23 years of age.

There is a very decided neurotic taint in all these cases. One of my cases occurred in a farmer's wife who stated that she was overworked and was anxious to have her husband move off the farm. The second patient was a country clergyman's wife. She ought to have been dissatisfied, but she did not say that she was. The third patient, already mentioned, a farmer's son who had been trying to get away from the farm for several years. He showed evidences of flushing on the slightest provocation and sweating of the palms of the hands. Two of the patients are well and one is dead.

I have been impressed especially by the description of the disease by Abel in his monograph published a few months ago, and by the treatment advised by A. J. Walton, of London, that is, manual divulsion through the stomach.

In the fatal case the patient died of an abscess of the lung with secondary empyema. She had a huge dilated esophagus. It is well known that a common mode of death in these atonic cases, in which there is great dilatation and accumulation of putrefied food, is inspiration from overflow during sleep. I cannot prove it, but I am inclined to think that the infection developed in the lung prior to operative intervention.

I believe that it is a bad plan to perform an operation in these cases until by gastrostomy one has restored the emaciated, dehydrated and nonresistant patient to the semblance of health

DR F A C SCRIMGER, Montreal, Canada I neglected the cardiospasm, because I still do not believe any spasm was present I should like simply to reemphasize what I believe to be the real danger In divulsion when you can have the material right on your hand and can see what you are doing, you can perhaps realize the dangers better than if the hand is introduced into the incision and the operation is done out of sight In the fatal case that I had it appeared to me that the patient could not have stood any kind of dilatation

# HYDATID CYSTS OF THE LUNG

REVIEW OF THE RECORDED NORTH AMERICAN CASES \*

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It is my purpose in this paper to call attention to the possibility of hydatid disease originating in American born persons and to collect the cases of the cysts of the lung due to infestation with *Taenia echinococcus* that have been reported in North America. In an address before the Clinical Congress of the American College of Surgeons at Montreal in 1926, Barnett<sup>1</sup> made the statement that hydatid disease is increasing so rapidly in some of the South American countries as to constitute a national peril. In 1922, N H Fairley<sup>2</sup> said that there had been no reduction during the preceding ten years in the number of cases admitted to the Melbourne hospitals. Many references can be found in the literature from the countries where infection with *Taenia echinococcus* is common showing an increased prevalence of the disease among the domesticated animals. Most of the known facts about this disease have come from the experience of such men as Deve, Dew Bird, Fairley, Barnett, Finochietto, Morquio, Escudero, Vegas Cranwell McKay and many others working in localities where the infestation is common. In spite of the vast amount of work being done in these regions represented by portions of France, Australia, New Zealand, Iceland, Italy, the Argentine and other South American countries, Spain and Germany, the disease has not been eradicated. This parasite exists in North America, and from time to time cases of hydatid disease have been reported in the natives of the United States and Canada. Of the 241 cases collected by Lyon,<sup>3</sup> 9 per cent occurred in persons born in America. In 68 cases that Magath<sup>4</sup> gathered from the literature between Lyon's report in 1901 and 1921, the incidence in native born persons was 5.9 per cent. In the group of 36 cases of hydatid cysts of the lung reported in this paper 2 occurred in persons known to have

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From the Department of Surgery, the University of Rochester School of Medicine and Dentistry and the Rochester General Hospital

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3 Lyon, I P. A Review of Echinococcus Disease in North America, Am J M Sc **123** 124, 1902

4 Magath, T B. Echinococcus Disease. Etiology and Laboratory Aids to Diagnosis, M Clin North America **5** 549, 1921

been born in the United States. Scattered reports of infestation among domesticated animals have appeared, but there has been, as far as I can determine, no concerted action to treat the situation with the thoroughness that its seriousness demands. The history of echinococcus disease in countries much more alive to its dangers than the United States shows no reason to expect natural diminution. Is there not reason to fear that this country is on the threshold of a period in which there will be a serious increase of hydatid disease among the native born population? There is surprisingly little information available as to the incidence of the infestation of animals in this country and Canada. *Taenia echinococci* have rarely been found in dogs in this country. In Washington, D. C., Curtice<sup>5</sup> recovered the parasite from a dog about forty years ago, and several years ago Kaup<sup>5</sup> in Kansas reported that it was found in dogs. Occasional reports of a search with negative results have been recorded. From 1877 to 1882, Osler<sup>6</sup> failed to find *Taenia echinococcus* in several scores of dogs examined in Canada. Swine are more commonly infested in North America than the other domesticated animals. In 1882, Osler and Clement,<sup>7</sup> in a study of the parasites in the pork supply of Montreal, were able to demonstrate infestation in 1 of every 33.4 examined. Lyon, in 1902, quoted Stiles, then zoologist of the Bureau of Animal Industry, Washington, D. C., to the effect that there was an undoubted increase in the incidence of infestation among domesticated animals. Johnston and Willis<sup>8</sup> reported several epidemics occurring in hogs in Virginia during 1913 to 1914. In one consignment of 46 hogs, from Charles City County which were slaughtered in Richmond, there was 100 per cent infestation. In another shipment of swine from Goochland County, 5 of 8 had hydatid cysts. In November, 1917, they reported 25 per cent of infestation in a shipment of 60 hogs from Charlotte County. These authors quoted Hall as saying "recent abattoir figures show an alarming increased prevalence of the disease in domestic animals in some parts of this country, notably in certain localities in Virginia, Arkansas and Oklahoma." Radcliffe,<sup>9</sup> in 1921, reported hydatid cysts in 100 per cent of a herd of 87 hogs. In a personal communication from Maurice C. Hall,<sup>10</sup>

5 Cited by Hall. Personal communication to the author.

6 Osler, William. Echinococcus Disease in America, *Am. J. M. Sc.* **84** 475, 1882.

7 Osler, William, and Clement, A. W. An Investigation Into the Parasites in the Pork Supply of Montreal, *Canad. M. & S. J.* **11** 334, 1882-1883.

8 Johnston, G. B., and Willis, M. Hydatid Cyst of the Liver with Report of Two Cases, *Surg. Gynec. Obst.* **25** 101, 1917.

9 Radcliffe, A. A. Infestation of a Herd of Swine by Hydatids, *M. Rec.* **99** 146, 1921.

10 Hall, Maurice C. Personal communication to the author.

chief of the Zoological Division, Bureau of Animal Industry, Washington, D C, it was stated that figures regarding the incidence of hydatids in domesticated animals in this country are not available "In general, it may be said that hydatids are not generally distributed throughout the United States and that they have a patchy distribution, not well known They are said to be prevalent in parts of New Mexico, Oklahoma and Arkansas, we can always obtain them on rather short notice from our inspection service at Richmond, Virginia, they are found from time to time at various abattoirs In 1927, Morris reported that they occurred in 5 per cent of swine at Baton Rouge, Louisiana, and that the former incidence was 20 per cent Di Jalen, our inspector at Cincinnati, Ohio, reported in 1927 that less than 1 per cent of swine at that station were affected" An attempt to ascertain the incidence of hydatid infestation in this portion of the country followed the discovery that one of the patients whose case is reported in this paper was born and has always lived in this locality A personal communication from P Olafson,<sup>11</sup> pathologist, New York State Veterinary College at Cornell University stated that he has failed to find the parasite during the past three or four years in the routine autopsy on approximately 1,000 of all species of the common domestic animals He further stated, however, that in pathologic specimens sent from the packing plants in Buffalo, the echinococcus cysts are occasionally included

Osler, in 1882, made the first collection of hydatid cysts in man in North America He was able to find 61 cases from recorded case reports, museum collections and personal communications This group included 5 pulmonary hydatid cysts Sommer,<sup>12</sup> in 1895, brought the list of recorded cases of echinococcosis up to 110 Up to July 1, 1901, Lyon collected 241 cases of which 45 per cent or 11 cases, showed pulmonary cysts In 1921, Magath added 68 cases from the literature and another 25 cases with hydatid disease that had been observed at the Mayo Clinic in the history of the institution Five of this group of 93 patients had hydatid cysts of the lungs Mills,<sup>13</sup> in 1925, made the statement that 18 pulmonary cysts were added to the literature since Lyon's report in 1902, but he did not give a list of the cases

In a search of the literature, I have been able to collect 34 cases of pulmonary hydatid cysts which, together with the 2 cases recorded in this paper, make the total of 36 known cases In this report are

11 Olafson, P Personal communication to the author

12 Sommer, H O Echinococcus Disease in the United States, New York M J 62 656, 1895

13 Mills, H W The Surgical Treatment of Echinococcosis, M J & Rec 122 407, 1925

included as cases of cysts of the lung instances that Lyon's paper classified as secondary invasion of the pulmonary tissue from the rupture of adjacent cysts, especially subdiaphragmatic. I have accepted as primary hydatid cysts of the lung all those cases with a fairly definite picture of an intrapulmonary cyst, whether or not there was evidence of multiple infestation of other localities in the body. Incidences of secondary involvement of the lungs, usually expressed by the expectoration of the hydatid elements following the penetration of the diaphragm and adherent lung by a cyst of the liver, are not included. Morton and I,<sup>14</sup> in a study of the literature of bronchobiliary fistula, found that the most common cause of this unusual condition was the rupture of an echinococcus cyst or an amebic abscess of the liver through the diaphragm into an adherent lung and thence into the bronchial tree. Neisser<sup>15</sup> said that 11 per cent of hydatid cysts of the liver break through into the respiratory apparatus. The acceptance of several of the cases herein reported may be questioned both as to the true nature of the pathologic process, because of the absence of the microscopic demonstration of scolices or hooklets, and because of the difficulty in determining the exact intrathoracic location, in several of which the cysts may have been pleural rather than pulmonary. Primary infestation of the pleura is rare. Neisser and Madelung<sup>15</sup> found 1.5 per cent in a collection of 1,179 cases of hydatid disease.

#### INCIDENCE OF PULMONARY INVOLVEMENT IN HYDATID DISEASE

Next to the liver, the lung is the most common organ to be invaded by *Taenia echinococcus*. Various statistics give the percentage of involvement of the lung up to 20 per cent. Greenway<sup>16</sup> collected 2,740 cases of hydatid cysts over a period of eleven years in which the incidence of pulmonary involvement was 14.69 per cent. In Algiers, Lavillat<sup>17</sup> found cysts of the lungs in 15.7 per cent of 210 cases. He quoted Lemaire who gave the incidence of 2,169 cases as 1.54, Prat, 1.35, and Finsen, 1.365. Vegas and Cranwell<sup>18</sup> reported an 8.5 per cent incidence of cysts of the lung, and Barnett found 10 per cent

14 Morton J. J., and Phillips, E. W. Bronchobiliary Fistula, Arch Surg 16: 697 (March) 1928.

15 Quoted by Lord, F. T., in Osler. Modern Medicine Philadelphia, Lea & Febiger, 1927, vol. 4, p. 285.

16 Greenway, D. J., cited in Foreign Letters (Buenos Aires) J. A. M. A. 79: 2019 (Dec. 9) 1922.

17 Lavillat Francis. Hydatid Cysts of the Lung with a Report of Five Cases, Internat. Clin. 2: 47, 1922.

18 Vegas, M. H. and Cranwell, D. I. Hydatid Cysts in Nelson's Loose Leaf Medicine New York Thomas Nelson & Sons 1920 vol. 2 p. 434.



of all cysts in the lung Dew's<sup>19</sup> figures are also 10 per cent for involvement of the lung

Multiple infection is common N H Fairley said "echinococcosis more often than not is a multiple infestation" K D Fairley,<sup>20</sup> in his study of 33 hydatid cysts of the lung in the Melbourne Hospital, found multiple organs involved in 39.4 per cent However, in a study of 112 cysts of the lung occurring in children, Morquio<sup>21</sup> stated that the cysts in most cases were primary and isolated In addition to the frequent involvement of other organs, multiple cysts occur in the lungs There may be many cysts in both lungs, apparently as the result of a secondary sowing from a primary cyst breaking through into the blood stream This is strikingly illustrated in Gurlee's<sup>22</sup> case in which the primary cyst occurred in the wall of the right auricle In the group of North American cases of cysts of the lung collected in this paper, there are only 6 that are conclusively multiple in the lungs There are 16 cases in which it is impossible to determine definitely, from a study of the records, the exact number of pulmonary cysts, although the probabilities favor a single cyst in the majority of these cases In 14 instances there seems to be sufficient evidence to judge that a single cyst was present

#### EVOLUTION OF A PULMONARY HYDATID CYST

The adult stage of the life cycle of *Taenia echinococcus* is lived in the upper intestinal tract of the dog and doglike animals This parasite is the smallest of the tapeworms, measuring only from 4 to 6 mm It possesses 4 segments, the terminal one of which produces large numbers of ova Barnett said that there are about 500 fertile ova in each ripe proglottis Innumerable ova are passed out with the excrement In one way or another these ova gain entrance to the body of the intermediary host It is most commonly stated that the infestation occurs through contaminated drinking water or vegetables that are eaten raw According to Barnett, the transmission is usually direct from the dog to the hands and hence to the mouth, in man, and sheep and cattle pick up the infection from contaminated herbage Deve<sup>23</sup> and Strawell<sup>24</sup> expressed the opinion that infestation occurs during infancy and child-

19 Dew, quoted by McKay, W J S M J Australia **1** 7, 1926

20 Fairley, K D The Results of an Analysis of Thirty-Three Cases of Hydatid Disease of the Lung, M J Australia **1** 341, 1922

21 Morquio, L Echinococcosis of the Lung in Children, Arch de med d enf **29** 72, 1926

22 Gurlee, C G A Case of Echinococcus Disease of the Heart and Lungs, Illinois M J **8** 85, 1905

23 Deve, F L'Echinococcose de l'enfant, Arch de med d enf **21** 225, 1918

24 Strawell, R R Symposium on Hydatid Disease, Brit M J **1** 673, 1927

hood This is the period when the greatest contact exists between the dog and human beings

Unlike *Taenia solium* and *Taenia saginata*, the larval stage of *Taenia echinococcus* occurs in the intermediate host The name, hydatid cyst, has been given to this larval stage as it occurs in man and in from 30 to 40 other mammals, most commonly sheep, swine and cattle Following ingestion, the embryo is freed from its protective covering by the digestive juices and, passing through the intestinal wall, enters either the blood stream or the lymphatic system By way of the blood stream, it may reach the lung through the general circulation or through the portal system The size of the embryo is from 20 to 25 microns (Biumpt), and it can traverse the capillaries by molding itself as do red blood cells (Lavillat) Neisser<sup>25</sup> advanced the theory that the embryo entered the thoracic duct and reached the general circulation at the subclavian vein Moiquio<sup>21</sup> suggested that the ova may reach the lung through the respiratory route It was formerly thought that the action of the gastric juice was necessary to liberate the ovum from its capsule However, Deve<sup>25</sup> showed that cysts may be produced by the subcutaneous implantation of ova, and, according to his opinion, the action of the leukocytes is sufficient to liberate the ova from its capsule The low percentage of pulmonary cysts in Iceland, where Finsen<sup>25</sup> reports 1 cyst of the lung for 365 cysts elsewhere in the body, may be taken as favoring this theory as Iceland is said to have a great deal of moisture with little dust K D Farley stated that the embryo reaches the lung by active migration and that it is improbable that the embryo is conveyed to the lung by the blood stream in any but occasional cases He based this conclusion from his study of a group of 33 cases, in 27 of which he found the hydatid cyst to occupy the lower portion of the right lung He also stated that the embryo usually reaches the liver through the blood stream, and then by active migration transports itself to the lung This theory is not supported by the figures of Heuser<sup>26</sup> who, in a study of 100 pulmonary cysts, found that the left lung was more frequently involved

The hydatid cyst develops from the embryo which has lodged in the pulmonary parenchyma The cyst consists of an outer lamellated very elastic cuticle and an inner parenchymatous or germinal layer Pulmonary cysts grow more rapidly than cysts elsewhere in the body because of the lack of resistance to expansion offered by the compressible lung tissue Escudero<sup>25</sup> stated that two years elapse from the time of infestation until there is sufficient growth to produce clinical symptoms As the cyst grows an adventitious layer of fibrous tissue

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<sup>25</sup> Quoted by Lavillat (footnote 17)

<sup>26</sup> Heuser C Hydatid Cyst of the Lung Am J Surg 4 486, 1928

forms from the host surrounding the invader. When the cyst has reached about the size of a walnut, blood capsules arise from the germinal layer producing great numbers of scolices. Dew<sup>27</sup> stated that a univesicular cyst is the typical morphology of hydatid disease, and that daughter cyst formation is a defensive reaction of the mother cyst against trauma, either mechanical, chemical or infective. The cysts of the lung usually do not contain daughter cysts. Dew reported only two with daughter cysts in twenty pulmonary hydatids. In examining hundreds from sheep he found three cysts of the liver and lung with daughter cyst formation. "Whenever an intrathoracic cyst is found to contain daughter cysts, an hepatic origin should be suspected and this should lead to an investigation of the diaphragmatic region" (Dew).

The fate of the enlarging pulmonary hydatid cyst depends on its nourishment, the effect its pressure causes on the surrounding tissues and its location within the lung. According to Dew, the cyst depends on osmosis for nutrition and consequently possesses a narrow margin of safety. The total lack of any evidence of connection between the endocyst and the adventitious fibrous layer of the host was strikingly illustrated at operation in my first case. Following removal of the fluid contents of the cyst by aspiration and the release of intracystic pressure, the endocyst was found lying free in the cavity formed within the pulmonary tissue. Bird<sup>28</sup> said that although obsolescence may occur, the majority of cysts rupture sooner or later. Erosion into a blood vessel is a common occurrence and occasionally may excite a fatal hemorrhage. Bird reported the cases of two patients who died in this manner. Rupture into a bronchus is the most frequent accident affecting the progress of the cyst's development. Finochietto<sup>29</sup> emphasized the importance of the localization within the lung in reference to the effect of rupture of the cyst into a bronchus. He recognized two groups as determined by their position in the lung, the central and the peripheral. The central cysts develop near the hilus and may be silent for a long time. Pressure gradually causes thinning of the bronchial wall finally rupture of the cyst takes place into the bronchus. The contents of the cyst are then expectorated, and if the opening into the air passage is sufficiently large, the germinal membrane may pass and recovery follow the retraction and cicatrization of the walls of the cavity. If the opening into the bronchus is too small to permit passage

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27 Dew H R. Daughter Cyst Formation in Hydatid Disease. Its Causation and Effects, *M J Australia* 2 497, 1925.

28 Bird, F D. Hydatids of the Lung, *M J Australia* 2 505, 1925.

29 Finochietto, E. The Treatment of Hydatids of the Lungs, *Practitioner* 119 10, 1927.

of the endocyst, infection occurs in the ruptured cyst and the picture becomes that of a bronchopulmonary suppuration. Bird said that infection within pulmonary cysts always follows rupture in contradistinction to cysts of the liver, which are frequently infected without rupture. The peripheral cysts involve the pleura soon causing pleural pain. Following rupture into a bronchus, according to Finochietto, the cyst near the periphery of the lung never evacuates its contents completely spontaneously, and cure by vomica cannot take place. Occasionally the cyst may rupture into the pleura or pericardium. After infection has occurred in the cyst, rupture into the pleural cavity results in pyothorax or pyopneumothorax. An uncomplicated cyst may rupture into the pleura, producing a hydrothorax, or if rupture into a bronchus is simultaneous, a hydropneumothorax occurs. Living scolices reaching the pleural cavity from the ruptured cyst of the lung may cause grafts to take place on the pleura. This happens rarely in pulmonary cysts. The metamorphosis of scolices into a new generation of cysts used to be termed a biologic heresy, but it is a common occurrence (Barnett). Dew<sup>30</sup> considered it an established fact that daughter cysts, brood capsules and scolices can implant themselves and form new hydatid cysts (fig 1).

#### SYMPTOMS

The symptoms of pulmonary hydatid disease vary according to the condition of the cyst. They may be divided into two groups, i. e., those produced by the uncomplicated cysts and those which follow rupture of the cyst. During the early period of the growth of the parasite in the lung, few if any symptoms are produced. Except for occasional anaphylactic phenomena, the echinococcus is well tolerated by the host until because of its size, pressure is made on surrounding structures. Loss of air space by compression of lung tissue results in shortness of breath. This occurs only when the cyst has reached a considerable size, as the normal vital capacity is so greatly in excess of the ordinary air requirement. Pressure on bronchi excites the cough reflex, and cough, slight or severe, is the commonest symptom. Erosion of the walls of blood vessels finally results in ulceration opening into the lumen of a vessel and hemorrhage into the bronchial tree follows. Hemoptysis is an important symptom in pulmonary infestation. Lavillat said that pulmonary cysts that have never given rise to hemoptysis may be considered as rare. In a series of thirty-eight pulmonary cysts Jauregui<sup>31</sup> found hemoptysis in 100 per cent. Pain, probably arising from pleural

<sup>30</sup> Dew, H. R. The Mechanism of Daughter Cyst Formation in Hydatid Disease. *M. J. Australia* **1**: 451, 1926.

<sup>31</sup> Jauregui, M. A. Hemoptysis Due to Hydatid Disease, *An. de Fac. de med. Montevideo* **12**: 681, 1927.

inflammation, may be mild or very severe. K. D. Fauley, in a study of thirty-three cysts of the lung, found cough in 100 per cent, hemoptysis in 57.6 per cent, pain in 54.4 per cent and dyspnea in 27.3 per cent of cases.

At the time of rupture there is a flooding of the bronchial tree with salt water, even to the extent of drowning. When a communication has been established between the cyst and the respiratory tract, the cough becomes more productive, and pieces of the wall of the cyst may

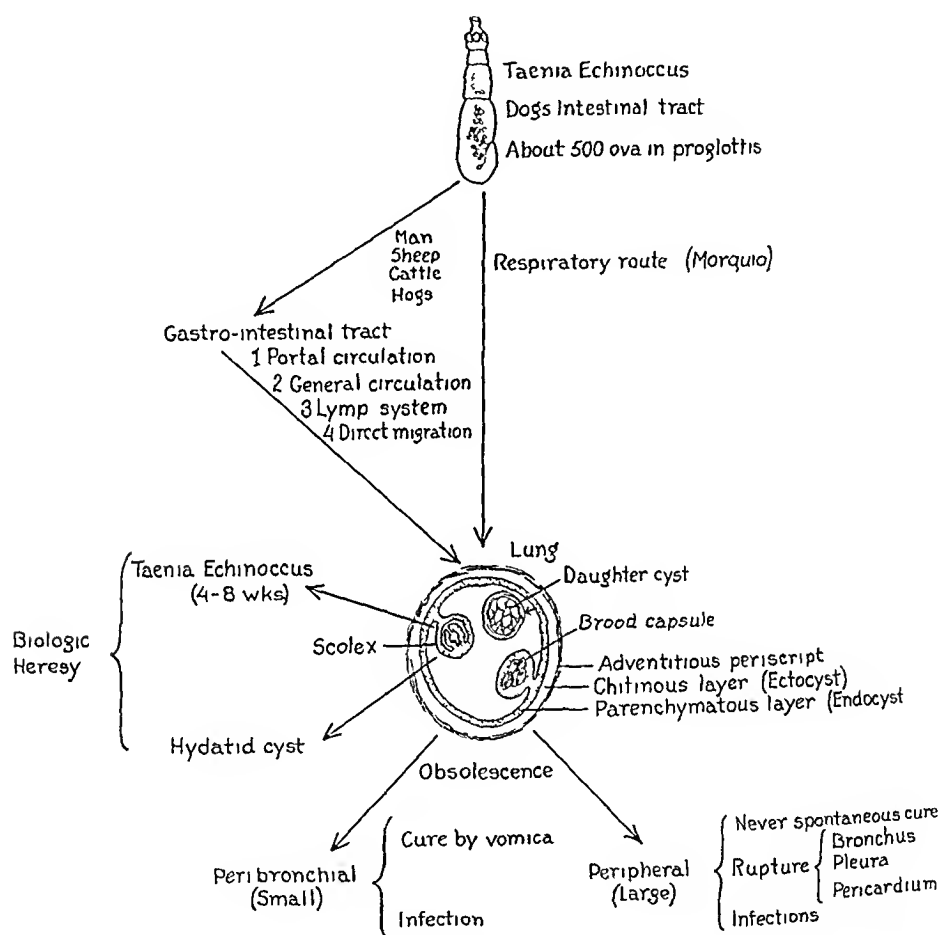


Fig. 1—Schematic representation of the evolution of a pulmonary hydatid cyst.

be expectorated. Infection usually follows rupture, and the picture becomes that of a bronchopulmonary suppuration with cough, purulent, foul-smelling expectoration, and the evidences of sepsis.

#### DIAGNOSIS

It is not surprising that many hydatid cysts are discovered at operation, the true nature of the pathologic process being unsuspected until some of the characteristic elements of the cyst are found. This is especially true in countries where the disease is rare and the possibilities of such a diagnosis are not kept constantly in mind. In the Mel-

bourne Hospital, according to Striawell, the diagnosis has been reduced to a 2 per cent error. This has been made possible by constantly considering this disease in differential diagnosis and by the employment of proved laboratory aids. In a study of 182 cases, however, N. H. Fairley found that a positive diagnosis was made in only 40.7 per cent. This series includes cysts located in various organs, in many of which the x-ray picture is not capable of rendering such valuable information as it does in the chest.

There are no pathognomonic symptoms of an unruptured pulmonary cyst, but a careful investigation of patients presenting the common symptoms of cough, shortness of breath, pain in the chest and hemoptysis should permit a correct diagnosis in the great majority of cases. Roentgenographic and fluoroscopic study of the chest is indispensable. The characteristic rounded or oval shadows, multiple or single, with clearcut edges, are to be confused with few other pathologic pictures.

Since Ghedini, in 1907, first applied a complement-fixation test as a diagnostic aid in echinococcosis, many clinical investigators have elaborated and perfected a technic which at present is used extensively in those countries where the disease is prevalent. Weinberg added much to make the test valuable, and it is frequently referred to as the Weinberg reaction and sometimes as the Ghedini-Weinberg test. There is not complete agreement as to the specificity of this test. N. H. Fairley did not find a positive reaction in 917 cases free from hydatid infestation and concluded that the complement-fixation test is absolutely specific. Le Nouene<sup>32</sup> quoted Tuffier and Deve as reporting positive reactions when echinococcus disease did not exist. Cottin and Saloz<sup>33</sup> reported a case of cancer of the liver in which a positive reaction was obtained to the echinococcus complement-fixation test. It seems safe to conclude that, though it may not be absolutely specific, the percentage of false positive reactions is so slight as to be negligible. In table 1 some of the results of the complement-fixation test are listed.

The intradermal skin test, commonly called the Casoni test after the originator, also has given excellent results as a diagnostic aid. It too apparently lacks absolute specificity. K. D. Fairley<sup>34</sup> in a study of eighty-seven positive reactions, was able to prove the presence of hydatid disease in only 59.8 per cent and he said that a positive reaction is not conclusive. Fernandez Ithurrat warned that the test may be positive in tuberculosis and in patients with a highly sensitive skin. In

<sup>32</sup> Le Nouene, Julien. A Clinical Study on Hydatid Pseudotuberculosis of the Peritoneum. *Internat. Clin.* 2:97, 1921.

<sup>33</sup> Cottin and Saloz. Reactions in Echinococcus Disease. *Arch. d. mal. de l'app. digestif* 13:1, 1923.

<sup>34</sup> Fairley, K. D. Intradermal Test in Hydatid Disease. *M. J. Australia* 1:472, 1929.

performing the test, he used from 0.2 to 0.6 cc of sterile centrifugated hydatid fluid (human, cattle or sheep), injecting it into the skin. Within a few minutes an erythema appears at the site of injection which spreads for one-half hour or longer. In from ten to fifteen minutes, an urticarial patch about 3 cm in diameter appears. Sette<sup>35</sup> prepared material for the intradermal test by evaporating 150 cc of hydatid fluid and mixing the residue with 10 cc of 0.9 per cent sodium

TABLE 1—*Complement-Fixation Test*

Author	Number of Cases	Percentage of Positive Tests	Comment
Weinberg, in Kolle and Wassermann <i>Hand buch der pathologischen Mikroorganismen</i> , ed 2, 1912, vol 1	306	82.0	
Zapelloni, quoted by Fairley <sup>2</sup>	500	93.0	
Fairley <sup>2</sup>	83	84.3	Reaction absolutely specific
Cignozzi <i>Riforma med</i> 38 485, 1922		93.0	
Ithurrat <i>J A M A</i> 79 2018 (Dec 9) 1922	187	88.0	
Greenway <sup>10</sup>		65.0	
Prado <i>Arch de clin med</i> 1 1, 1925	48	92.31	Weinberg test never fails him
Lozano <i>J A M A</i> 80 1533 (May 26) 1923			
Mogena <i>Arch españ de enf del aparato digestivo</i> 7 345, 1924	14	73.0	
Horowitz Wlassowa <i>Deutsche med Wehnsehr</i> 52 113, 1926	20	90.0	Negative in 62 controls
Dew, Kellaway and Williams <i>M J Australia</i> 1 471, 1925		92.0	
Cantani <i>Riforma med</i> 45 1577, 1929			A low percentage of error

TABLE 2—*Cason Intradermal Skin Test*

Author	Number of Cases	Percentage of Positive Tests	Comment
Mogena <i>Arch españ de enf del aparato digestivo</i> 7 345, 1924	4	100.0	
Trenti <i>Policlinico</i> 31 353, 1924			Superior to other biologic tests
Deuseh <i>Deutsche med Wehnsehr</i> 51 1305, 1925			Much more dependable than complement fixation test
Finochietto <i>J A M A</i> 82 1376 (April 26) 1924		99.0	
Makhas and Assimakopoulos <i>Zentralbl f Chir</i> 55 1793, 1928	61	91.8	Uncomplicated cysts
Fairley <sup>34</sup>	13	53.8	Suppurative cysts
		77.0	Uncomplicated cysts
		92.6	Ruptured or suppurative cysts
Cignozzi <i>Riforma med</i> 38 485, 1922		90.0	
Itharrut <i>J A M A</i> 79 2018 (Dec 9) 1922		98.46	
Dew <i>Brit M J</i> 1 673, 1927		90.0	

chloride and 20 cc of glycerol. He used 0.1 cc of this preparation in performing the test. Some of the results obtained with the intradermal test are given in table 2.

Magath found that three patients proved by operation to have hydatid cysts reacted positively to a skin hypersensitivity test. He made three small abrasions in the skin on two of which he placed hydatid fluid from a patient or from a sheep leaving the third abrasion for a

<sup>35</sup> Sette, N. Intradermal Test for Hydatid Disease, *Policlinico* 32 1175 1925

control Within twenty minutes a raised white wheal appeared surrounded by a zone of redness There was no itching The lesions subsided in about three hours This test seems simple, rapid and readily interpreted and should prove to be a help in the diagnosis of hydatid disease

A satisfactory result of any of the biologic tests used to aid in the diagnosis of echinococcosis depends entirely on the activity of the material with which the test is performed A laboratory with an abundance of hydatid cysts passing through it can be sure of having satisfactory hydatid antigen In this country, where only an occasional hydatid cyst is seen, most localities are not equipped to perform these tests properly Horowitz-Wlassowa said that the hydatid antigen spoils in from four to five months Settle claimed that by the method he uses in preparation, material for intradermic tests will keep active for as long as a year

The significance of a positive reaction persisting after the surgical cure of a hydatid cyst has not been definitely determined Weinberg<sup>36</sup> stated that "the specific antibodies disappear slowly from the blood stream of patients operated upon for hydatid cysts" He found a positive reaction up to six years and three months after operation, but admitted that the interpretation should be reserved when the reaction is positive after several years Le Nouene quoted Laubry and Parou to the effect that the antibody disappears from the blood in from three weeks to six months after the removal of the cyst, and that a persistence of a positive reaction after six months means that a cyst has been overlooked or that there is a recurrence N H Farley regarded a strongly positive reaction after twelve months as absolutely diagnostic of another cyst Kelloway<sup>37</sup> expressed the opinion that with the Casoni test both immediate and delayed reactions would continue for years following the death or surgical cure of the parasite Deusch also said that the Casoni test remains positive for a long time after the removal of the cyst The statement has been made by Dew, Kelloway and Wilhams that the complement-fixation test may be positive in cured patients sixteen years after operation

While an increase in the number of eosinophil leukocytes in the circulating blood may occur in hydatid disease eosinophilia does not exist often enough to be of any considerable value in the differential diagnosis K D Farley<sup>29</sup> spoke of it as inconstant Cantani said that eosinophilia in hydatid disease is inconstant and lacks specificity Mogena found eosinophilia in 54 per cent of fourteen cases Eosinophilia in from 60 to 80 per cent was reported by Cignozzi

<sup>36</sup> Weinberg quoted by Le Nouene (footnote 32)

<sup>37</sup> Kelloway C H Symposium on Hydatid Disease Brit M J 1 673 1927



Following the rupture of a pulmonary hydatid cyst, the so-called complicated cyst, additional diagnostic aids are available. The story told by the patient should frequently excite suspicion. Following a chronic cough, probably associated with hemoptysis and possibly with pain in the chest, the patient, during a coughing spell, finds the air passages flooded with a profuse watery expectoration which has a salty taste. Portions of the wall of the cyst or some of the contents of the cyst may be found in the sputum when there has been rupture into a bronchus. Probably hooklets from degenerated scolices are the commonest hydatid elements found in the sputum. However, daughter cysts and pieces of the wall of the cyst have been expectorated. Fragments of the wall because of inherent elasticity, tend to curl up and assume a shape which has led them to be called daughter cysts. Lavillat reported a patient who coughed up "grape skins," but at operation no daughter cysts were found within the mother cyst. When communication has been established with the air passages, air may enter the cyst, giving the picture described as a "pneumocyst." If the cyst has not completely emptied its contents, a fluid level will be observed on the x-ray film. Rupture into the pleura may give the appearance of pleurisy with effusion, and if rupture into a bronchus has been simultaneous, air may enter the pleural cavity, giving the picture of hydro-pneumothorax. Deve<sup>38</sup> collected and reported a series of thirty-one cases with this complication. As shown later, the consensus condemns exploratory puncture as a diagnostic measure in hydatid disease, but in cases seen for the first time following rupture into the pleura, with the appearance of a hydrothorax or a hydropneumothorax, exploration with a needle seems a logical step. On the recovery of a fluid "limpid, like spring water" or resembling cerebrospinal fluid, the diagnosis of a hydatid cyst should be considered. Microscopic examination of the fluid may reveal scolices or hooklets. When infection has supervened, the case resembles a bronchopulmonary suppuration and becomes more difficult of diagnosis, although a search of the sputum may reveal the characteristic hydatid elements.

As one reads the reports of cases of pulmonary cysts, it is seen that exploratory aspiration for diagnostic purposes is resorted to fairly frequently. The expressions from those having the greatest experience in hydatid disease universally disapprove of this step. Dew<sup>27</sup> said that the exploratory puncture is rarely practiced now. He warned that it may be followed by a secondary sowing of cysts, and that the exploratory puncture of even a small cyst is dangerous. McKay<sup>39</sup> stated that

38 Deve, F. Hydatid Gas Cyst of the Lung, *Rev de chir* 63 245, 1925

39 McKay, W. J. S. Hydatid Cysts of the Lung and Their Surgical Treatment, *M. J. Australia* 1 7, 1926

the use of a needle and syringe must be forbidden because of the danger of infecting the cyst. Lavillat condemned the exploratory puncture. He said that it may provoke a violent anaphylactic intoxication with rapid death. K. D. Fairley<sup>20</sup> emphasized the danger of exploratory aspiration.

#### TREATMENT

There is no medical treatment for pulmonary hydatidosis. Various chemical substances have been tried, both clinically and in experimental animals, without demonstrating any value. Lolli<sup>40</sup> showed by his experiments in rabbits that neoarsphenamine does not influence in the least the course of echinococcus disease. He stated that no therapy, unless its efficacy has been proved in animal experimentation, should replace surgical intervention. Morquio said that medical treatment is of no avail. Deve<sup>41</sup> asserted that vaccination therapy, as advocated by Petroff, is ineffectual. Claims have been made that the effect of the roentgen rays is beneficial. Deve and Billiard<sup>42</sup> concluded from their experience in its clinical use and in experimentation with laboratory animal infestations that roentgentherapy has no curative action. In Balboni's<sup>43</sup> second case no change in symptoms, roentgen appearance or in the complement-fixation test followed roentgenotherapy.

Expectant treatment, because of the possibility or likelihood of spontaneous cure apparently is a debated question. Morquio said that expectant treatment is preferable, and that most cases of hydatid cyst in the lungs of children are cured by vomica. In his experience, in 90 per cent of the cases in which rupture into a bronchus occurs spontaneously the patients recover. Deve advised watchful waiting if the cysts are small and deep in the region of the hilus or if there has been a vomica. He also said that 90 per cent of cysts rupturing into a bronchus will terminate in recovery. Pereira<sup>44</sup> reported the cure of six of seven pulmonary cysts through spontaneous evacuation. Corvetto<sup>45</sup> collected in Lima, Peru thirteen instances of pulmonary cysts in eight of which the patients coughed up the membrane and were cured, two were cured by operation and three died. On the other

40 Lolli, G. Medical Treatment of Echinococcus Cyst, *Polichinico (sez. med.)* **36** 601, 1929.

41 Deve, F. Vaccination Not Effectual in Echinococcosis, *Compt. rend. Soc. de biol.* **91** 933, 1924.

42 Deve, F. and Billiard, A. Hydatid Cysts and Radiotherapy, *Compt. rend. Soc. de biol.* **91** 848, 1924.

43 Balboni, G. M. Hydatid Cyst of the Lung. *Boston M. & S. J.* **187** 879, 1922.

44 Pereira, E. P. *Arch. latino-am. de pediat.* **17** 1, 1923.

45 Corvetto, A. Parasitic Disease of Lungs in Peru. *An. de Fac. de med. Montevideo* **5** 196, 1922.

hand Dew<sup>47</sup> said that all patients with hydatid cysts should be operated on as soon as a diagnosis is made. Bird stated that operation is the only treatment. Prat<sup>46</sup> warned not to rely too much on the possibility of cure by vomica, as it occurred only twice in his forty-three cases. From a study of the various opinions expressed regarding the indications for operation it would seem that small central cysts warrant a policy of watchful waiting, but that peripheral cysts of any considerable size require surgical intervention without too long a delay.

Therapeutic aspiration is reported by Mirailhe<sup>47</sup> to be a dangerous procedure. He collected forty-three cases in which aspiration was employed. There were two cures, twenty-two deaths and ten negative results. The dangers incident to aspiration were discussed under diagnosis. It is safe to assume that the puncture of a hydatid cyst is contraindicated until the cyst has been exposed at operation and the field has been properly protected so as to prevent leakage of hydatid fluid into the pleural cavity.

The plan of surgical attack in pulmonary hydatid cysts must be varied so as to meet the condition of the cyst when it comes to operation. The uncomplicated cyst is an entirely different problem from the cyst that has ruptured into a bronchus and is secondarily infected. Complete agreement does not exist as to the best method of surgical treatment in the case of unruptured cyst. Syme<sup>48</sup> said that the ideal treatment is complete extirpation of the cyst and closure of the chest without drainage. Finochietto<sup>49</sup> stated that uncomplicated cysts may be removed and the wound closed without drainage. He quoted Pasados as having reported seventeen cases in which operation was performed in this manner in 1898. He never operates in two stages and empties the cyst by holding the wall of the cyst outside of the chest cavity because of the danger of secondary hydatidosis when one scolex or several remain behind. Local anesthesia is advocated by Finochietto. Bird operates in one stage, and after the removal of the endocyst depends on the condition of the adventitious pericyst for the indications for drainage. If there is no adventitious layer he closes the lung and chest without drainage. When the cavity is held open by thickening of the pericystic layer, he employs drainage for forty-eight hours. In cases with a thick adventitia, he sutures it to the pleura and drains until the cavity is obliterated. Nasseti<sup>50</sup> closes the chest without drainage after obliter-

46 Prat, D. Curative Vomica in Hydatid Cyst of the Lungs, *An de Fac de med*, Montevideo **10** 161, 1925

47 Mirailhe, quoted by Crow, L. B. *Am J Roentgenol* **5** 513, 1918

48 Syme, George. Symposium on Hydatid Disease *Brit M J* **1** 673 1927

49 Finochietto, E., cited in, *Foreign Letters (Madrid)*, *J A M A* **82** 1376 (April 26) 1924

50 Nasseti, F. Treatment of Hydatid Cyst Without Drainage, *Arch ital di chir* **12** 125, 1925

ating the cavity within the lung by drawing the walls together with sutures. K. D. Fairley<sup>20</sup> operates in one stage and sutures the pleural layers if adhesions do not exist. McKay does not believe that a two-stage operation is advisable. He uses intratracheal anesthesia to render positive pressure. After suturing the adventitia to the edge of the wound, he opens the cyst and it is emptied of the fluid contents and the endocyst. He always drains the cavity for a short time so as to prevent occurrence of a subcutaneous emphysema. Antonucci<sup>51</sup> suggested the obliteration of the lung cavity by approximating the opposing walls with suture and closure of the chest wound without drainage. He then compresses the lung by an artificial pneumothorax. In 1925, Mills said that the consensus favored the use of a two-stage operation, called the Lamas-Piat-Mondino technic. This operation consists in a rib resection under local anesthesia with a tampon of iodized gauze placed against the parietal pleura as a first stage. This stage is followed in about ten days by an opening into the cyst without the use of anesthesia.

The method of injecting formaldehyde into the cyst at operation before incising it to remove the contents, as advocated by Deve, does not seem applicable to pulmonary cysts because of the dangers of flooding the bronchial tree with the solution.

Surgical measures in common use in pulmonary suppuration are found to deal satisfactorily with infected, ruptured pulmonary cysts. Harvey<sup>52</sup> reported a case in which he obtained a cure in an infected cyst through the use of an artificial pneumothorax. Pneumotomy with removal of the contents of the cavity and drainage until the cavity has become obliterated is the method of treatment commonly practiced. In 1898, J. B. Murphy<sup>53</sup> stressed that a suppurating cyst should be treated like a pulmonary abscess and opening into the lung should wait for fixation of the lung to the thoracic wall. Finochietto<sup>49</sup> has boldly depended on bronchial drainage after cleaning out an infected cyst cavity and completely closing the incisions in the lung and chest. When thick-walled cavities remain after prolonged drainage some method to secure their obliteration must be attempted. Campbell<sup>54</sup> reported the cessation of the cough and expectoration following phrenectomy in a case in which an infected cavity remained after a two-stage operation for a suppurating hydatid cyst. K. D. Fairley<sup>20</sup> mentioned the necessity of removing several ribs in order to obliterate a cavity. In my first case it was necessary to unroof the cavity by removing the thickened

<sup>51</sup> Antonucci, C. Hydatid Cyst of the Lung. *Polichinico (sez. prat.)* **30** 798, 1923.

<sup>52</sup> Harvey, Cotter. Suppurating Hydatid Disease of the Lung Cured by Artificial Pneumothorax. *M. J. Australia* **1** 458, 1929.

<sup>53</sup> Murphy, J. B. Surgery of the Lung. *J. A. M. A.* **31** 341 (Aug. 13) 1898.

<sup>54</sup> Campbell, A. I. Diaphragmatic Paralysis is a Therapeutic Measure in Intrathoracic Disease. *Quart. J. Med.* **21** 463, 1928.

parietal pleura and underlying adherent lung, together with the ribs and intercostal tissues. This allowed the superficial thoracic wall to drop into the pulmonary cavity, where it finally became adherent and permitted healing to take place.

#### PROGNOSIS

In 1882, Osler said, "The accidental ingestion of the eggs of the tiny *Taenia echinococcus* of the dog produces the most serious and fatal parasitic disease of man." Echinococcosis as a disease is responsible for a great many deaths in those portions of the world where it is common. Curran and Locke<sup>55</sup> made the statement that 14 per cent of the death rate in Iceland during 1917 was due to echinococcus cysts. The prognosis in pulmonary hydatid cysts depends mainly on whether or not there is multiple infestation as a complication. Solitary cysts or even the presence of multiple invasion of pulmonary tissue, provided the extent is not too great, should not carry a high mortality. Because of the increasing diagnostic aid offered by the biologic tests and the use of the fluoroscope and the roentgen rays, both for help in differentiation and for localization, pulmonary cysts do not present serious difficulties in diagnosis. The great advances made in intrathoracic surgery during the past few years has made it possible to develop surgical methods of handling hydatid cysts of the lung with a minimum of operative risk. In the series of thirty-three cases studied by K. D. Farley,<sup>20</sup> death resulted in four, or 12.12 per cent. Operation was not performed in ten of these cases, there was apparent cure by vomiting in eight and death in two, or a mortality of 20 per cent. There were two deaths in the twenty-two patients on whom operation was performed, giving a mortality rate of about 9 per cent. Heuer<sup>56</sup> quoted Garré as reporting an 80 per cent cure by open incision in a collection of ninety-nine cases, and Tuffier, who collected thirty-five cases treated by operation, reported only one death. These figures are comparable to statistics quoted by Lavillat. He mentioned that Pasquier reported recovery in 85.18 per cent and Guimbellat in 87 per cent.

#### REPORT OF CASES

CASE 1—*History*—Miss F. L., a stenographer, aged 19, was first seen at the Highland Hospital on Feb. 21, 1929. She was born in Delevan, N. Y., and at the age of about 3 years was brought to Rochester. She had never traveled out of her native state. For several years, the patient had a pet dog which during the last few months of its life suffered from some gastro-intestinal disturbance. It died suddenly during the summer of 1928, as other dogs in the same neighbor-

<sup>55</sup> Curran, J. F., and Locke, A. W. *Echinococcus Cysts*, Boston M. & S. J. 191 932, 1924.

<sup>56</sup> Heuer, G. J. *Surgery of the Lung*, Nelson's Loose Leaf Surgery, 1927, vol. 4, pp. 5 and 584.

hood had, and its death was attributed to poisoning. The patient had had scarlet fever at 17 years of age, otherwise she had been well up to the onset of the present illness.

In February, 1928, she had an attack of pleurisy associated with fever and disability. She did not remember which side was involved. In March, there was a recurrence of pleurisy which lasted about a week. About June 1, there was another attack of pleurisy, for the treatment of which she entered the Genesee Hospital on June 11, where she remained for several days. A study of the hospital record reveals that 60 cc of clear opalescent fluid was obtained by aspiration of the left side of the chest, the fluid was negative on culture and on inoculation into a guinea-pig. The blood showed a persistent leukocytosis of from 20,000



Fig 2 (case 1)—Roentgenogram showing a large uncomplicated hydatid cyst in the lower part of each lung field

to 30,000. There was no increase in eosinophils. Roentgenograms of the chest showed large oval shadows with clearcut edges in the lower part of each lung field (fig 2). The diagnosis of pulmonary echinococcus cysts was suggested as a possibility by Dr D B Jewett, because of the roentgen appearance. However, the patient was discharged from this hospital at her own request and was lost from observation by the staff.

Following discharge from the Genesee Hospital, she gradually improved but did not entirely recover her strength. Unproductive cough persisted. About five weeks before admission to the Highland Hospital she had a violent coughing spell, during which she coughed up a large quantity of pus and blood with an extremely offensive odor. Since that time she had had a persistent cough productive of about two cupfuls of very foul sputum in twenty-four hours. Associated with

these symptoms were evidences of sepsis with fever and loss of strength, appetite and weight

*Examination*—On admission to the Highland Hospital, physical examination revealed a pale, undernourished girl, obviously seriously ill. She had a distressing cough and raised much extremely foul-smelling, purulent sputum. Other than the poor general condition, nothing abnormal was found except on examination of the chest. The heart was not displaced. On the right side there was impaired resonance, front and back, in the lower portion of the chest. In the area of dulness there were diminished breath sounds. No râles could be heard. On the left side there was dulness beginning at the angle of the scapula. This changed to absolute flatness in the lower part of the chest. The breath sounds were absent over the

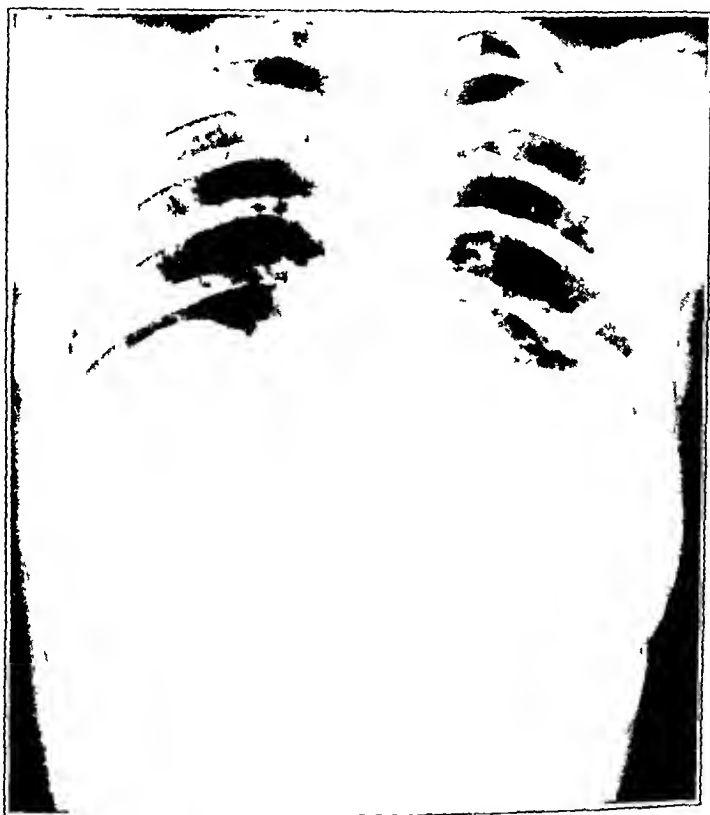


Fig. 3 (case 1)—The hydatid cyst on the left has become infected. On the right side, the shadow of the cyst merges with the diaphragm and interpretation is rendered difficult.

area of flatness and markedly diminished in the area of dulness, and there were many moist râles in this region.

Urinalysis was negative for sugar or albumin. The sputum was negative for tubercle bacilli. No search was made for hydatid elements. The blood count showed leukocytosis without eosinophilia.

Roentgenograms made at this time differed markedly from those made about seven and a half months previously at the Genesee Hospital. (It was not my privilege to study the earlier films until after I had operated on this patient.) On the left side, there was complete obliteration of the lower portion of the lung field by a uniform shadow. On the right, there was obliteration of the lower portion of the lung field by a shadow consistent with a high placed diaphragm (fig. 3). Iodized poppy seed oil 40 per cent injected into the lower portion of the

left lung field showed an uneven distribution of the material, which did not suggest bronchiectasis, but rather that the oil had entered an abscess cavity and was mixed with its contents (fig 4)

*Operations Course*—On Feb 22, 1929, with the patient under procaine hydrochloride anesthesia, a subperiosteal resection of about 3 inches (7.6 cm) of the left tenth rib posteriorly was performed. The parietal pleura was thickened and hard. Careful dissection through it resulted in entrance into pulmonary tissue, showing the parietal and visceral layers of the pleura firmly adherent. On aspiration of the indurated lung, pus was recovered about 1½ inches (3.7 cm) from the surface. The intrapulmonary cavity was opened with the cautery. There was a cavity about the size of a large orange which contained pus of extremely offensive



Fig 4 (case 1)—The distribution of iodized oil through the area of suppuration in the left base

odor that quickly permeated the entire operating floor. Further exploration of the cavity revealed that it contained a large amount of partially degenerated membrane and small circular pieces of a similar nature—all collapsed and not unlike empty grapeskins. The cavity was thoroughly emptied and drainage tubes were inserted. The external wound was held open by a gauze pack. Hooklets of the echinococcus scolex were found in the pus from the cavity.

Following operation, there was rapid improvement in the patient's general condition. The cough and expectoration disappeared. There was progressive gain in weight and strength. However, after several months' observation, there was apparently no reduction in the size of the intrapulmonary cavity and the persistence of many open bronchi annoyed the patient. It finally became obvious that spon-



taneous obliteration of this cavity was not going to take place, and the patient was admitted to the Rochester General Hospital on July 7, for treatment of the residual cavity and bronchial fistulas

On July 8, with the patient under procaine hydrochloride anesthesia, a plastic operation designed to obliterate the remaining thick-walled intrapulmonary cavity was performed. A curved incision with convexity downward passing at lowermost limits about 3 inches below the scar and sinus of former operation was made. The skin and superficial thoracic wall were dissected upward forming a flap. The external wall of the cavity, consisting of ribs, intercostal bundles, thickened parietal and visceral pleurae and the fibrosed pulmonary tissue, was excised to the limits of the cavity. The skin flap was allowed to fall into the cavity, over the bronchial fistulas, and was held in place by a gauze pack.

Following this operation, healing was slow, but finally the skin flap became adherent to the surface of the lung. The open bronchi were frequently cauterized



Fig 5 (case 1) —The deformity of the lower left side of the chest resulting from operations. The shadow of the cyst on the right is still consistent with a shadow cast by a high diaphragm

with silver nitrate during this period. During December, the healing was complete, and the bronchial fistulas were all closed. Roentgen study at this time showed deformity of the wall of the lower left part of the chest, but it was felt that there was sufficient functioning pulmonary tissue on the left side to warrant an open operation on the right side of the chest for removal of the hydatid cyst in the lower part of the right lung, which had remained unruptured and uninfected (fig 5).

On Jan 16, 1930, with the patient under gas-oxygen anesthesia supplemented with local infiltration and nerve block with procaine hydrochloride, about 8 inches (20.3 cm) of the right eighth rib was resected subperiosteally. The pleura was incised, and the chest was opened for the full length of the incision. The seventh rib was sectioned at the anterior and posterior ends of the incision to obtain a better exposure. There were a few stringlike adhesions between the visceral and

parietal pleurae, and a small amount of lymph was present on the pleural surfaces. The upper and middle lobes were pink and normal in appearance. In the lower lobe of the lung there was a mass larger than a child's head, shaped somewhat like a football. It was firm and tense. Where it approached the surface of the lung it was white and cartilaginous in appearance. The lung overlying the cyst was of a deep wine-red color, almost a purple. The chest was carefully walled off with gauze packs, and the cyst was aspirated and emptied of its fluid content through a gallbladder trocar. The fluid was perfectly clear and resembled "spring-water." As the cyst emptied, the lung was grasped with clamps and delivered from the chest. An incision was made through the pericystic layer, and the hydatid cyst was removed by grasping it with sponge forceps. It was lying free within the pericyst without connections or adhesions to the host. The cavity within

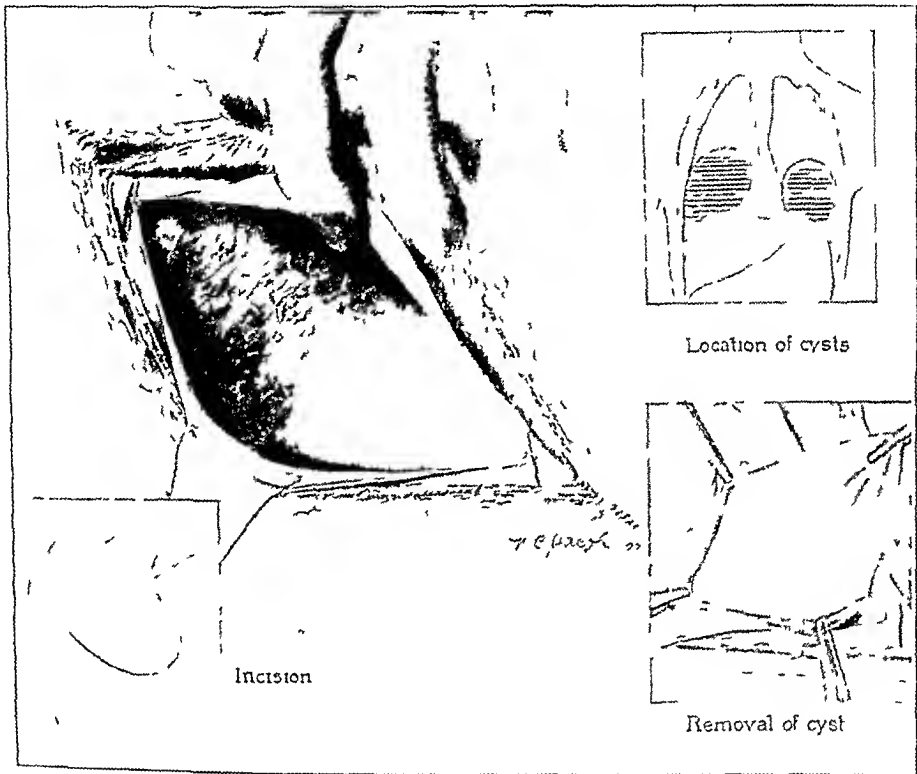


Fig 6 (case 1) —Transpleural approach to a large cyst in the right lower lobe

the lung was carefully cleaned out by aspiration and sponging, and through the incision into it, was marsupialized to the skin. The remainder of the incision in the chest was closed by suture in layers, resulting in air-tight closure. The operation was well borne (fig 6).

No daughter cysts were found. The fluid from the cyst contained many brood capsules, scolices and hooklets (fig 7).

For the first few days, the patient was moderately dyspneic, and there was slight cyanosis. There was only a moderate elevation of temperature, but the pulse rate varied between 120 and 140 for several days. There was a slight amount of bloody drainage from the marsupialized area and for about four weeks the patient could express air from the cavity within the lung on cough or deep breathing. The incision healed without infection. After three weeks she began

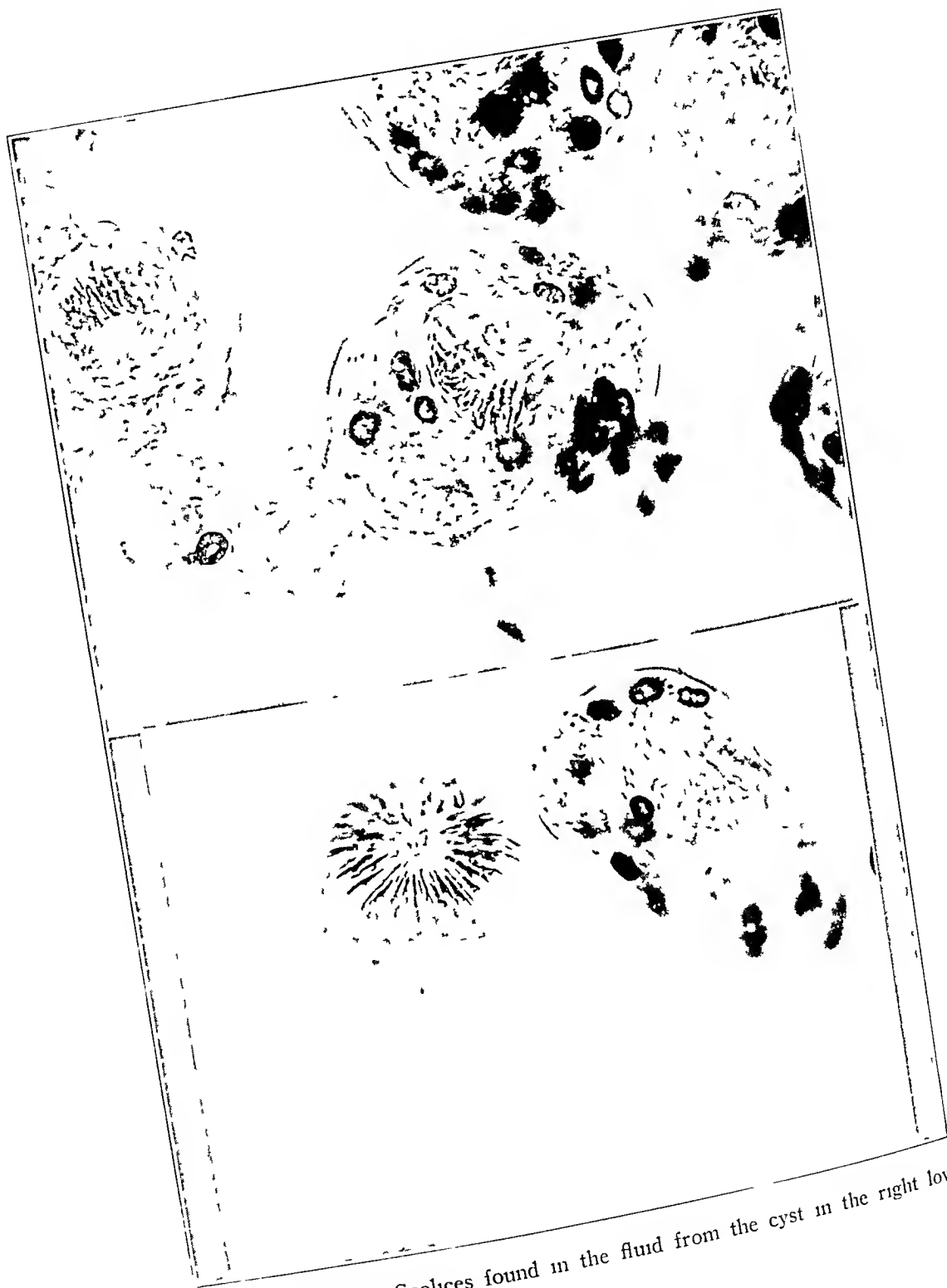


Fig 7 (case 1) —Scolices found in the fluid from the cyst in the right lower lobe

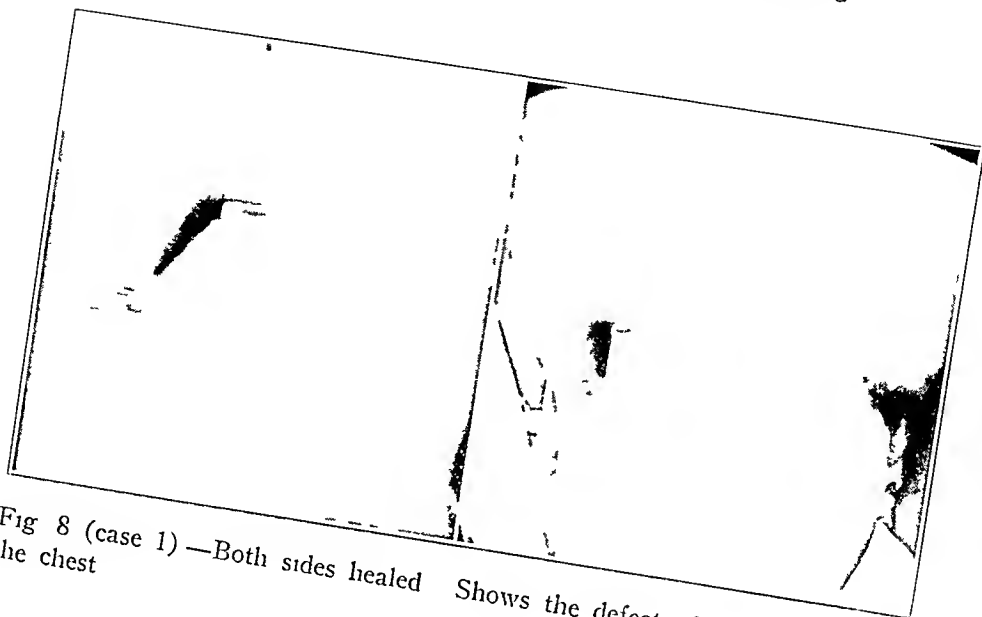


Fig 8 (case 1) —Both sides healed Shows the defect of the lower left wall of the chest

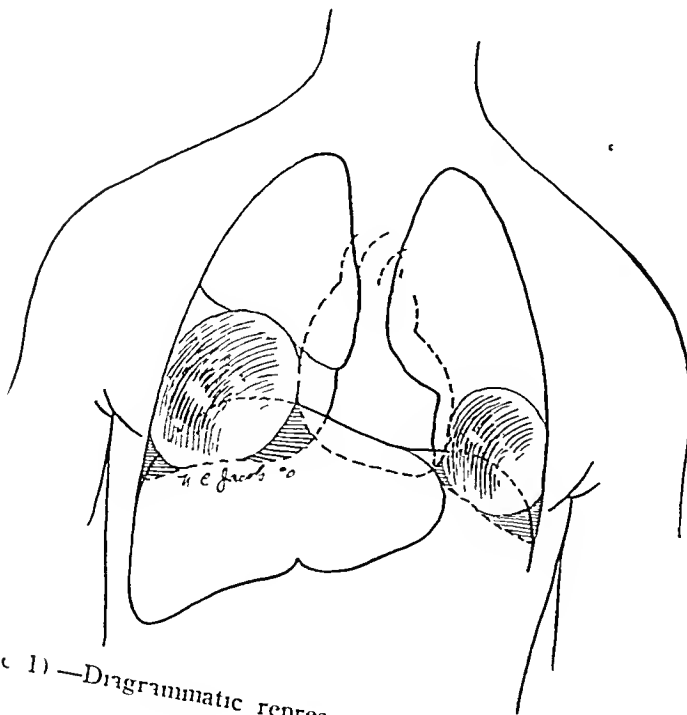


Fig 9 (case 1) —Diagrammatic representation of the relative position of the hydatid cysts

to get up out of bed. At first there was some dyspnea on exertion, but this gradually cleared up, so that at present she has no shortness of breath. She has progressively gained in strength and weight (fig 8).

About two months after the last operation, an intradermal skin test performed with echinococcus antigen prepared from the contents of the patient's hydatid cyst provoked no immediate reaction, but there was a delayed reaction in the form of an erythematous area about 4 cm in diameter, which appeared in about eighteen hours and persisted for two days.

*Summary*—A large hydatid cyst was present in the lower lobe of each lung. The cyst on the left side ruptured into the bronchial tree and became infected. The suppurating cyst was removed through pneumotomy, and a secondary plastic operation was necessary to obliterate the residual fibrosed lung cavity. The cyst on the right remained unruptured and did not become infected. It was removed by a one-stage operation, and recovery followed.

Dr James M. Markin of Rochester referred this patient to me (fig 9).

*CASE 2—History*—Mr. B. A., an Italian, aged 35, was admitted to the Rochester General Hospital on Dec. 9, 1927, because of pain in the right side of the chest, cough and hemoptysis. In Italy, he had lived on a farm and had tended sheep and cattle. He had a dog at that time. He came to the United States about sixteen years ago. During the World War, he served with the army in France for about nine months. He had scarlet fever while in Italy, but aside from this had been well until the onset of his present symptoms. For about ten years he had had pain in the right side of the chest and a chronic cough. There had been some expectoration, at times of a black color. Occasionally he had noticed blood in the sputum. He had had some dyspnea, and occasionally suffered from night sweats. His appetite was good, and he had not lost weight. About one week before admission to the hospital, he felt feverish and had increased dyspnea. He consulted his physician, who found a large shadow in the right side of the chest on fluoroscopic examination, and the patient was sent to the hospital for study and treatment.

*Examination*—The patient was an obese Italian. The temperature on admission was 101 F, pulse rate, 98, and respiratory rate, 22. Nothing abnormal was found on examination except for the chest. There was no bulging or retraction of the thoracic wall. The expansion was limited over the right side. The percussion note was dull over the right side of the chest, especially posteriorly. Over the back, the breath sounds were absent, and they were considerably diminished in the axilla and over the front of the right side of the chest. There were no rales. The left lung was clear throughout. The heart was not displaced, the heart sounds were of fairly good quality and there were no murmurs.

Urinalysis gave entirely negative results. The red blood count was 4,630,000, and the hemoglobin reading, 91 per cent (Sahli). The white blood count was 8,300, polymorphonuclears, 70 per cent, lymphocytes, 27 per cent, transitionals, 2 per cent, and eosinophils, 1 per cent. The Wassermann and Kahn reactions of the blood were negative. Roentgen examination was performed by Dr. L. R. Lingeman, who reported a large dense shadow occupying the lateral aspect of the right thoracic cavity. This had a sharp, clearcut medial margin and a homogeneous density throughout. He felt that it was necessary to consider in the differential diagnosis, a large encysted pleural effusion, a malignant condition of the pleura and echinococcus cyst of the lung (fig 10).

An intradermal injection of an echinococcus filtrate caused no reaction either immediate or delayed. (This filtrate was about a year old and I have no knowl-

edge as to its antigenic content Presumably it had lost the power of provoking a reaction)

*Operation*—On December 12, with the patient under gas-oxygen anesthesia supplemented with infiltration and nerve block with procaine hydrochloride, a long segment of the right ninth rib was excised Many adhesions existed between the lung and the parietal pleura, which were separated by finger dissection There was a large cystic tumor in the right lower lobe reaching from the diaphragm high into the chest The external wall of the cyst was thick and fibrous and showed some calcification The cyst was aspirated, and grayish-red fluid was obtained It gave somewhat the appearance of a suspension of gold-dust The



Fig 10 (case 2) —Roentgenogram showing large, dead cyst of right lower lobe

wall of the cyst was incised, and a large amount of the same fluid escaped, together with degenerated tissue not unlike fibrin The external wall of the cyst was excised as far as it could be reached There was no evidence of open bronchi on the inner wall of the cyst The cavity was packed with gauze, soaked in acriflavine 1:500 and the anterior end of the incision was closed in layers

*Pathologic Report*—The fluid and pieces of the wall of the cyst were examined by Dr I Gaspar who reported that the fluid contained many cholesterol crystals Several smears of the centrifugated sediment were examined, but no hooklets were found Section of the wall of the cyst showed a marked hyaline fibrosis There were no bronchial glands and no deposit of hemosiderin pigment in the wall He concluded that the etiology of the cyst could not be definitely determined, but it is possible that it was a fairly old echinococcus cyst

*Course*—The postoperative period was complicated by a prolonged febrile reaction. Immediately following operation, the temperature rose, fluctuating between 102 and 103 F and remained at this level for ten days, when it increased to between 103 and 105 F, it persisted at this height until the nineteenth day, when it fell to between 100 and 101 F, at which level it continued for several weeks. During this time the pulse ranged from 110 to 130. This was thought to be the result of infection in the pleural cavity. The drainage from the chest became purulent and rather foul. Following the institution of irrigation with surgical solution of chlorinated soda (Dakin's solution), the foul odor disappeared and the nature of the drainage changed. A transfusion of 500 cc of citrated blood was given once following operation as the red blood cells had fallen to 3,720,000 with a hemoglobin reading of 71 per cent. On Jan 12, 1930, the cavity within the chest held 500 cc of surgical solution of chlorinated soda. The use of 'blow-bottles' was started, and the patient was encouraged to use them frequently. By February 9, the size of the cavity had decreased so that it overflowed on instillation of 185 cc of the surgical solution. On February 13, it was necessary to enlarge the sinus tract under local anesthesia as the tract had become so narrowed as to prevent adequate drainage. Serial roentgenograms showed a progressive although slow, decrease in the size of the residual cavity. On April 17, a roentgenogram showed only a narrow unobliterated cavity. The lung showed definite expansion. The cavity held but 45 cc on April 30. The patient's general condition remains excellent.

*Summary*—The patient presented a large cyst in the right side of the chest. It was treated surgically by removal of the contents and excision of the greater part of the external wall. There were no scolices or hooklets found in the cyst's contents. I believe that this case represents one of a large hydatid cyst which had terminated its growth by obsolescence. In favor of this opinion are the long course of the typical symptoms of a hydatid cyst of the lung, the roentgenologic appearance and the operative observations, all of which are difficult to explain on any other basis.

#### CASES REPORTED IN THE LITERATURE

GAY'S CASE<sup>57</sup> (1858)—D. R., a man, aged 71, had always been well until February 1857. The symptoms in the illness preceding his death were entirely bladder difficulties. There was no mention of pulmonary symptoms or signs. Autopsy showed a carcinoma of the bladder. "At the apex of the left lung was a layer of white, dense, fibrous tissue an inch in diameter, and between one or two lines in thickness. The surface in the immediate neighborhood was rendered opaque, with thin patches of the same. Beneath a dense white substance was a layer of pulmonary tissue of about the same thickness, and within this a cavity upwards of  $\frac{1}{2}$  inch in diameter filled with serum and lined by a thin bluish-white membrane which was everywhere studded with yellowish-white points. Most of the serous fluid was lost. That which remained was of a yellowish color and contained a large number of echinococci, detached hooks and a few concentric corpuscles. The lining membrane itself was covered with the same parasites. It presented the usual striated appearance."

*Summary*—A man, aged 71, died from carcinoma of the bladder. Autopsy revealed a hydatid cyst of the left lung unrecognized during life. The diagnosis was proved by recovery of hooklets and echinococci.

<sup>57</sup> Gay Case Report, Boston M & S J 57 218, 1858

STILLE'S CASE <sup>58</sup> (Credited to Gay by Lyon) —At a meeting of the Pathological Society of Philadelphia, a cyst was exhibited about three-fourth inch (1.8 cm) in length, pyriform and containing yellowish-red fluid. This was expectorated shortly before death by a man whose main symptoms were great emaciation and cough, and who presented dulness on percussion and a feeble respiratory murmur of the right lung, at the apex of which gurgling also existed. There was no postmortem examination and no proof as to the nature of the cyst.

*Summary*—A cyst was expectorated shortly before death by a man presenting pulmonary symptoms. This case is included by Lyon in his series as a pulmonary hydatid cyst. The record makes acceptance questionable.

SMITH'S CASE <sup>59</sup> (1858) —Mrs. A., aged 34, from girlhood had had symptoms of a diseased liver. At intervals of one or two years there were acute paroxysms of pain accompanied by enlargement. In the winter of 1857, growing tenderness was noted in the hypochondriac region. The side was swollen even to distortion of the ribs. Much pain and numbness in the arm and foot of the right side were constant symptoms. Early in April, 1857, the disease became more acute. The swelling of the side, the pain and the soreness increased rapidly. There was great pain in the top of the head with acceleration of the pulse. Without premonitory symptoms of any kind, there was a large discharge from the bowels of fetid, purulent and bloody matter which continued for two and a half days, producing great exhaustion. Cough set in with expectoration of frothy fluid at first, and later sputum resembling that of pneumonia. About September 1, cysts were first coughed up, from one to three in a day, varying in size from that of a filbert to that of a pea, all much torn. They were examined by more than one observer, and not a trace of parasite was found. The discharge of cysts became gradually less frequent but more numerous and more variable in size. Sometimes after an interval of five days, twenty or thirty would be thrown off at one paroxysm of coughing that lasted two or three hours. Later these paroxysms occurred once in ten days, and the cysts were discharged perhaps during the course of two days. Some were so perfect as to have but one aperture, they were inflated by the blow pipe. Some smaller than a pea came up unbroken, but soon collapsed. Their contents were apparently purely serous, and the same thick expectoration as at first accompanied them. The cysts were opaquely white—with few exceptions, the walls were translucent—and under the microscope exhibited only occasional striae. At the time this case was reported the patient had much less pain and suffering than she had the winter before, though she was not so strong and respiration was more deficient. The specimens of sputum contained some clots of blood. The paroxysms were exhausting, violent and spasmodic, resembling those of whooping cough.

*Summary*—A woman, aged 34, whose birthplace was not mentioned, apparently had a large cyst of the liver which ruptured into the gastro-intestinal tract. There was also primary infestation of the lungs with a cyst rupturing into a bronchus and partially discharging its contents. The numbness in the arm and the foot on the right side together with the intense headache suggests also a cyst involving the central nervous system. The case was reported as "cysts from the liver coughed up through pulmonary passages." The case is included in Osler's series as an instance of echinococcus cyst of the lung.

<sup>58</sup> Stille. Case Report, *North Am Med & Chir Rev* 2:506, 1858.

<sup>59</sup> Smith, F. Gurney. Case Report, *North Am Med & Chir Rev* 2:333, 1858.



**MINOT'S CASE**<sup>60</sup> (1859) —A woman, aged 35, for several years had had pain shooting to the back and to the right shoulder and uneasiness in the right hypochondriac region. In the spring of 1856, while in New Orleans, she was seen by a physician who detected an obscure tumor in the right hypochondriac region, which he described as feeling like a watch, deeply seated beneath the integuments. At this time she had considerable prostration. In April, 1857, a large tumor developed rapidly in the same spot. It embarrassed respiration and compressed the right side of the lung so that no respiratory murmur could be heard, except in the upper part of the right side of the chest. It was excessively painful and tender. One night she had several enormous evacuations from the bowel, the discharge being clear, colorless fluid and excessively fetid. The tumor almost wholly disappeared at once. She was extremely prostrated and had considerable fever, from which she slowly recovered. About June 1, she began to cough and to expectorate frothy mucus. About September 1, she began to cough up hydatid cysts of various sizes. This occurred about twice a week, two or three being discharged each time, with a sensation as if they were detached from the lower part of the right lung. The tumor diminished, and in October could no longer be felt. The patient's health steadily improved, and on Sept. 27, 1859, she was quite well. She had not coughed up any hydatid cysts for three months.

**Summary** —A woman, aged 35, whose nationality was not known, had a large cyst in the upper right part of the abdomen which discharged into the gastrointestinal tract. Her condition was later complicated by the expectoration of hydatid cysts, over a period of many months. This case was reported by Leon as a case of hydatid of the liver with perforation of the diaphragm and the lung. A study of the case record suggests multiple infestation of the lung and liver.

**LOOMIS' CASE**<sup>61</sup> (1878) —A man, aged 43, a native of Ireland, a shoemaker, at the age of 19 had his first attack of inflammatory rheumatism, which lasted two months and involved all of the large joints. He had several similar attacks at intervals of from one to four years. The length of attacks varied from one to three months. In September, 1867, he suffered from unusual cardiac palpitation accompanied by severe paroxysms of coughing, and for the first time in his life he raised blood. The spitting of blood continued almost without interruption until Jan. 10, 1878. The blood was bright red and varied in quantity from 1 to 2 teaspoonfuls. During this time, he raised some blood nearly every day. On January 10, he began to spit up much larger quantities than ever before. From January 10 to 18, he thought that he raised as much as 18 pints of blood. On January 18, after a violent fit of coughing, he raised something that had the appearance of a membrane. It was pearly white and partly red. Following this, he raised other pieces, some of which looked like little sacs. Each time he expectorated a piece he would spit up a large quantity of bright red blood. During the period of profuse hemorrhage, he lost weight rapidly and became very weak. Three weeks after the first profuse hemorrhage he again coughed up membrane and had another severe hemorrhage. At this time he felt as though something was torn out of the inside of his chest. The membrane came up in quite large pieces and he experienced a sense of relief. Since then he raised no blood or membrane. At the time this case was reported he coughed a little and had a slight amount of mucopurulent expectoration. He gained steadily in weight and

60 Minot. Case Report, Boston M & S J 61 279, 1859

61 Loomis, A. L. Hydatids of the Lung, M Rec 14 281, 1878

strength Palpitation, which had troubled him more or less for the past two or three years, was less than at any time since that period

He generally looked quite well The pulse and temperature were normal On examination of the chest, the right shoulder was found to be lower than the left, and there was slight retraction on the right side, more marked posteriorly than anteriorly Motion of the right side during respiration was markedly diminished The apex of the heart was plainly visible 1 inch (2.5 cm) to the left of its normal position Vocal fremitus was more marked on the right, especially in the mammary and superior axillary regions There was loss of resonance all over the right side of the chest, being most marked in its lower portions Exaggerated respiration was heard all over the left lung On the right side below the nipple there was almost absence of respiratory sound On a line with the nipple, bronchial breathing was heard over the right infrascapular space

There was hypertrophy of the heart with mitral regurgitation and stenosis The lower margin of the liver was palpable below the costal margin It was smooth and rounded The spleen was slightly enlarged on percussion No tumor was palpable in the abdomen The sputum contained portions of the wall of the hydatid cyst and in some instances a complete hydatid cyst There were minute white particles within the cyst Under the microscope, they proved to be 'echinococcus homonomus'

Dr Loomis concluded that it was probable that at the time of his examination there were no cysts in the lungs, as the patient had had neither hemorrhage nor pulmonary symptoms since he last expectorated a cyst about four weeks before

*Summary*—A man, aged 43, a native of Ireland, suffered from cardiac hypertrophy with mitral stenosis and regurgitation Apparently spontaneous cure occurred by rupture into the bronchus and expectoration of the cyst However a four weeks' follow-up seems insufficient to prove a spontaneous cure The diagnosis was proved by microscopic discovery of "echinococci homonomus"

AINSWORTH'S CASE<sup>62</sup> (1880)—MAN Stearns, Polish, aged 40, was admitted to the Post Hospital, Fort Vancouver, in the latter part of August, 1875 The history and physical examination gave indications only of urinary and abdominal disease On the fourth day after admission symptoms of acute general peritonitis developed, and the patient died on September 12

Autopsy revealed general peritonitis The bladder was completely filled with cysts, about sixty, varying in size from that of a pinhead to that of an orange The cysts were lying free in the bladder They were all single The bladder also contained a much larger sac, ruptured, which was considered to be the mother sac

The middle lobe of the right lung contained, embedded in its anterior portion, a tumor a little larger than a walnut, consisting of a firm, fibrous, yellowish-white capsule intimately connected on all sides with the pulmonary tissue and containing several cysts varying in size from that of a pea to that of a marble There was also a cyst in the lower extremity of the spleen about the size of an orange, similar in external appearance to the one in the lung There is no mention of a microscopic examination

*Summary*—A man, aged 40, Polish, died of general peritonitis No pulmonary symptoms had been noted Hydatid cysts of the bladder, spleen and middle lobe

<sup>62</sup> Ainsworth F C A Case of Hydatids of the Bladder, M Rec 18 346 1880

of the right lung were found at autopsy. The diagnosis was not proved by microscopic study, but the gross description seems satisfactory proof.

FENGER AND HOLLISTER'S CASE<sup>63</sup> (1881) — Francesco Coputa, an Italian, aged 34, a laborer, was a patient in the Cook County Hospital. Twelve years before, while a mounted gendarme in Italy, he suffered from a hemorrhage from the lungs of about 2 ounces (56.7 Gm). He was hospitalized for one week. During the next two years, he remained well. After this time he had a cough accompanied by pain around the right nipple. The pain subsided on the application of leeches and the cough also disappeared after a month. In the following years, every autumn he had a return of the pain, always at the same point in the chest, between the third and fifth ribs and around the nipple, accompanied by coughing. This would persist for a month but was relieved by the use of leeches and venesection. During the past four years the pain became more severe, as did the accompanying cough. In the interval between attacks he would occasionally feel some pain in the region of the right nipple when lifting a heavy weight. He came to New York in 1870, where he stayed one and a half years. He worked during this time except for the period in the fall in which he had his usual attack of pain and cough, during which he expectorated mucous matter which was occasionally slightly streaked with blood. In July, 1880, he came to Chicago, where he commenced work as a common laborer. During September, the pain in the right nipple set in again. It was a steady unvarying, intense pain, accompanied by a slight cough. His appetite remained good, but he was forced to stop work for two weeks. In November, he had a recurrence of pain and cough and had to stop work. He lost his appetite, became weak, and for the three weeks prior to admission to the hospital was confined to bed. During this time cough distressed him day and night, and in the twenty-four hours he raised about 1 pint of mucous matter, sometimes streaked with blood. Suddenly, about one week before entrance to the hospital, he coughed up a large quantity of whitish material, as he said "white, like paper." Cough and pain increased. He grew weaker, lost his appetite and was unable to sleep. He was told by those about him that his breath was offensive.

Physical examination showed a poorly nourished man, tall and of moderate weight, with profuse perspiration. The pulse rate was 98, the temperature 104 F and respiratory rate 36. When he lay on his back and the chest was percussed, he coughed incessantly, and a very offensive odor was noticed around the bed.

Percussion showed dulness below the second rib anteriorly on the right side. There was also dull percussion in the axillary and infra-axillary regions and over the scapular and interscapular regions. When the patient lay on his back, there was an area of tympanitic percussion on the anterior side of the body. Both sides of the chest participated equally in the respiratory movements. The right side of the chest was neither sunken nor prominent. The intercostal spaces had the same appearance on the right as on the left side. In the region of the dull percussion note, the tactile fremitus was nearly, but not quite, absent. Over the right side of the chest, sibilant rales were heard in the upper part of the upper lobe and in the posterior part of the lower lobe over the regions of the dull percussion, respiratory sounds were obscure. When the patient lay down there were cavernous respiratory sounds over the tympanitic area. The anterior part of the right side of the chest near the nipple line was aspirated with the patient sitting up, and thin, grayish fluid of the same offensive odor as the breath was withdrawn. On microscopic examination, the fluid contained a large number of pus cells with fatty detritus and bacteria.

63 Fenger, Christian and Hollister, J. H. Opening and Draining of Cavities in the Lungs, *Am J M Sc* 81:378, 1881.

The diagnosis was fetid cavity of the middle lobe of the right lung near the anterior surface and most superficial at the nipple, having an insufficient outlet through a large bronchial tube in the anterior border of the cavity, and diffuse, purulent bronchitis in the left lung. Operation was performed by Dr Fenger on December 26, with the patient under ether anesthesia. An incision  $2\frac{1}{2}$  inches (6.27 cm) long was made in the third intercostal space,  $1\frac{1}{2}$  inches (3.7 cm) to the right of the sternum. The incision was carried down, exposing the intercostal muscles. A detached hypodermic needle was introduced, and as neither inspiration nor expiration caused this to move, it was withdrawn and the incision carried into the cavity. About one-half pint of grayish-white offensive matter mixed with some air escaped. The opening was then enlarged to allow entrance of the finger into the cavity. Digital exploration revealed firm tissues toward the axilla, and in this region between the fifth and sixth ribs a counter opening was made. A heavy rubber tube, 10 mm in diameter, was now passed from the anterior to the posterior opening. The cavity was irrigated with 2 per cent carbolic acid. As soon as the cavity was filled, the patient began to cough. During coughing it was noticed that a yellowish-white mass would appear at and protrude a little from the anterior opening. This was removed. It was one large coherent gelatinous mass. On microscopic study, this proved to be a large echinococcus cyst. The wall of the cyst presented the characteristic finely striped, that is, laminated, layers of amorphous or homogeneous substance, the stripes always running parallel to the surface of the wall. The sac was from about 5 to 6 inches (12.7 to 15.2 cm) in diameter. The wall was homogeneous, gelatinous and transparent. It was soft and friable, but still somewhat elastic, and presented no secondary cysts. On Feb 6, 1881, the incisions were healed, and the patient had no cough or expectoration. On April 7, he was discharged from the hospital as cured.

*Summary*—An Italian, aged 34, had pulmonary symptoms of twelve years' duration. There were cough, pain in right side of the chest and hemoptysis. The cyst ruptured into a bronchus, and this was followed by suppuration within the cyst. Pneumotomy was performed, and recovery ensued. The diagnosis was proved by the microscopic examination, although there is no mention of the discovery of scolices or hooklets. This is the first recorded case of suppuration of the lung cured by pneumotomy.

*SMITH'S CASE*<sup>64</sup> (1882)—A girl, aged 20, was first seen on Nov 4, 1881. Her chief complaint was a running sore on the posterior part of the chest. This was situated opposite the eighth intercostal space on the left side 2 inches (5 cm) from the spine. Several sinuses were found running upward and outward. There was no other bulging on the chest. She did not have cough, pain or shortness of breath. The duration of symptoms was two years. Symptoms began with pain in the left side followed by slight shortness of breath and very little cough, but no expectoration. Occasional chills, fever and sweating were noted. After six months a tumor as large as a closed fist developed near the inferior angle of the scapula. It had been diagnosed and treated as a fatty tumor, cold abscess, etc. On two or three occasions it was opened and pus escaped. Operation was performed on November 30, with the patient under chloroform anesthesia and the sinuses were laid open by an incision extending from the sixth to the ninth ribs. A probe could be made to pass deeply through the small openings in the sixth seventh and eighth intercostal spaces. Two transverse incisions  $1\frac{1}{2}$  inches long were then

<sup>64</sup> Smith D F. Case Report Canad M & S J 11 195 1882

made in the intercostal spaces, and a considerable quantity of dirty, brown pus escaped. The finger could now easily be passed through around the intercostal slit, and the costal walls of the cavity were felt to be smooth, regular and unyielding. Injection through the upper openings resulted in pus and a number of small, smooth and slippery-walled cysts of different sizes being forced through the lower opening. The cysts were all opened when they escaped, and they quite collapsed, none was larger than a marble. Some of the cysts still contained a small quantity of slimy, semitransparent, glairy fluid. No microscopic examination was made. The patient progressed well, and recovery was complete in two months.

*Summary*—A girl, aged 20, presented slight pulmonary symptoms. The thoracic wall was penetrated by a suppurating cyst from within the left pleural cavity. There was no definite proof that the disease originated in the lung. It may have been a pleural cyst (fig 11).

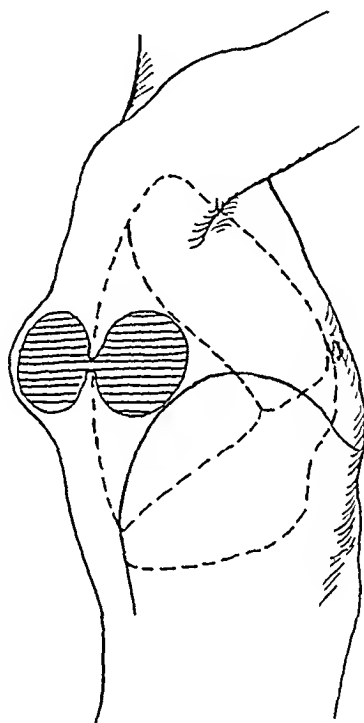


Fig 11 (D F Smith's case)—Spontaneous penetration of the thoracic wall by a suppurating cyst

BERNAY'S CASE<sup>65</sup> (1882)—This was the case of an Englishman, who had come from Honolulu, who expectorated an echinococcus from the lungs.

*Summary*—This case was not published and was recorded in the foregoing brief manner in Osler's series of cases. Lyon credited the case to Bernay, but the reference given was to Osler's compilation of case reports, in which Bernay's case is included.

BLACK'S CASE<sup>66</sup> (1882)—A minister, a native of Essex County, England, had been in Canada about six years. He first consulted Dr Black in November, 1878. He gave a history of gradually failing health for four years. In 1876, Dr Atkins

<sup>65</sup> Bernay. Case Report, *Am J M Sc* 84 475, 1882.

<sup>66</sup> Black. Case of Echinococcus Disease of the Lung, *Canad M & S J* 11 140, 1882.

of Toronto had discovered and removed a hydatid tumor of the liver. For a time he was improved, but the improvement was not lasting. During a year and a half prior to this consultation, he was steadily less fit for attending to his duties. The patient was much emaciated and of sallow complexion. His countenance had a pinched and somewhat cachectic appearance. He had some dyspnea with a dry cough. The epigastrium and right hypochondriac region were tense and somewhat tender. The lower intercostal spaces on the right were enlarged and tense. There was marked dulness over the lower part of the right lung. The heart was in normal position and greatly deficient in force. The spleen was slightly enlarged. The lateral margin of the liver was large, hard and smooth. There was increasing dulness in the right side of the chest. The spleen increased in size rapidly. Dyspnea became more marked. Some edema of the feet developed. On Feb 25, 1879, after a distressing coughing fit, he raised nearly 2 pints of purulent fluid, in which floated a large number of cysts varying in size from 2 to 3 inches

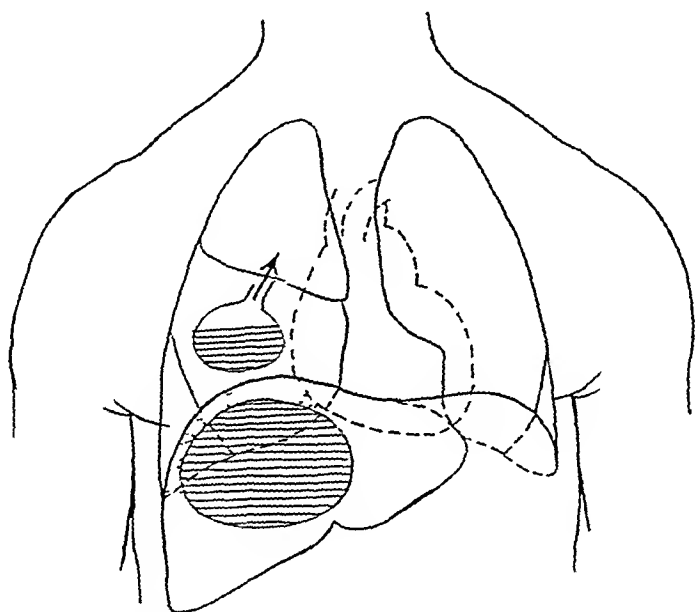


Fig 12 (Black's case) —Cyst in the right lower lobe communicating externally through a bronchus, large unruptured cyst of the liver

in diameter to those barely perceptible. Following this, there was daily purulent expectoration and some cysts. Gradually the symptoms improved. On March 10, he had succeeded in raising a cyst larger than any of its predecessors. When "giving a sudden cough, purulent material began to boil out of his mouth and nostrils and he was strangled instantly."

Autopsy revealed "abscess of the lower part of the right lung which had been distinct from that of the liver. The purulent matter and cysts discharged on February 25, and from that time until the tenth day of March, I believed to have been the contents of this abscess. The cavity was flooded by a greenish-yellow purulent fluid and floating cysts discharged from the hepatic abscess. The heart was lying with its apex to the left nearly beneath the left sternoclavicular articulation. The upper part of the right lung was studded with tuberculosis. The left lung was in its normal condition. The diaphragm was pushed far up into the thorax, the liver was adherent to the diaphragm, and through the diaphragm

was a large opening which communicated with an immense cavity in the liver. The rupture of the diaphragm and the consequent discharge of the contents of the hepatic abscess I believe to have been the immediate cause of death. The cavity in the liver was about  $9\frac{1}{2}$  inches in depth and 6 inches across. In the cavity was still a large quantity of greenish-yellow fluid like that found in the chest. The liver was of immense size and studded with tubercles of a yellowish color many of which were about the size of a pea. The spleen had imbedded in it a large cyst filled with colorless fluid in which I could detect no scolex."

*Summary* —A man, age not given, a native of England, had been in Canada for six years. A large hydatid cyst of the liver and a large hydatid cyst of the right lower lobe of the lung were found. The cyst of the lung ruptured and discharged through a bronchus, following suppuration. The infected cyst of the liver ruptured

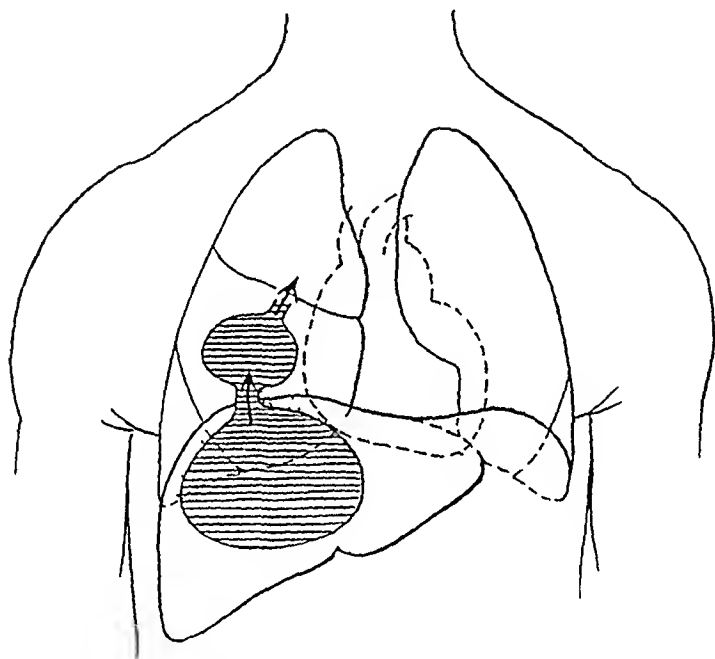


Fig 13 (Black's case) —The cyst of the liver penetrated the diaphragm and lung, emptying into the intrapulmonary cyst and causing death

through the diaphragm into the pulmonary cyst, causing sudden death of the patient by drowning (figs 12 and 13)

FERGUSON'S CASE<sup>67</sup> (1893) —In a patient dying from cancer of the stomach, a large cyst was discovered post mortem. "He did not complain of his lungs and a cyst, a small one, was first discovered on the postmortem table."

*Summary* —A cyst of the lung was discovered at autopsy. There was no microscopic proof of the nature of the cyst. Probably Ferguson's classification of this cyst as a hydatid cyst is satisfactory proof, as he had a fairly extensive experience with hydatid infestation among immigrants from Iceland who had located in Winnipeg. He reported having seen twenty-one cases of hydatids of the liver and six others in which hydatid cysts were located in other organs.

<sup>67</sup> Ferguson A. H. Hydatids of the Liver, Northwest Lancet 13 41, 1893

KEYES and BUSCH'S CASE<sup>68</sup> (1896)—A German, aged 53, of extremely intemperate habits, had had typhoid fever in 1865 and some liver trouble in 1872, at which time, according to his statement, he passed a quantity of black marbles, probably gallstones. His last illness dated from January, 1895. On March 17, he came under the care of Dr. Hebenstreit and Dr. Meisbinger, who obtained the following history. The patient had pain in the right side near the liver. He coughed up a grayish fluid of a disagreeable odor, and an acid taste. The right side of the chest was bulging. The right pleural cavity was aspirated, and one syringeful of serous fluid was removed. A small tumorlike mass, which could be felt just below the ensiform cartilage and to the right, was also explored with a hypodermic needle with negative result. On percussion, the liver did not extend below the free border of the ribs. It extended as high as the nipple in front and at the same level to the median line behind. In the axillary line there was flatness extending to the crest of the ilium. The patient died on March 16, 1896.

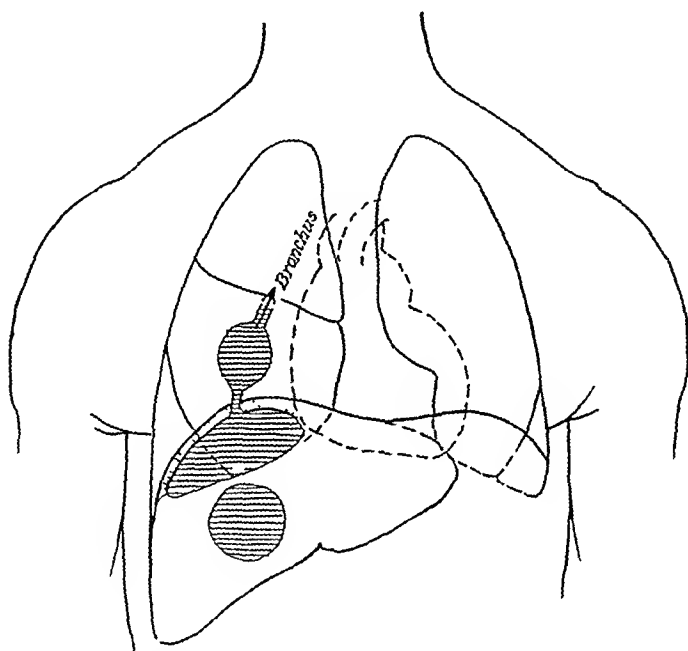


Fig 14 (Keyes and Busch's case)—Intrapulmonary cavity communicating with a large cavity in the subphrenic region, also an unruptured cyst of the liver

Autopsy revealed no fluid in the pleural cavities. The left lung was normal. The right lung was firmly adherent at the base to the diaphragm. It crepitated well. On section, bloody froth exuded from the bronchial tubes. A cavity with calcareous walls was discovered in the base of the lower lobe, 50 mm in breadth and 10 mm in depth. It communicated with the bronchus on one hand, and on the other, through an opening in the diaphragm with a similar though much larger cavity immediately below the diaphragm which measured 100 mm in its horizontal diameter and was 15 mm in depth. It was also lined by calcareous plates. No opening could be discovered leading from it, except that into the lung cavity. Immediately beneath this subdiaphragmatic cavity, there was still another. It was partly surrounded by liver tissue and was intimately connected to the gall-

<sup>68</sup> Keyes, W. C., and Busch, F. C. A Case of Multiple Echinococcus Cysts, Buffalo M. J. 35: 25, 1896.



bladder and its ducts by inflammatory adhesions. Its capacity was about 100 cc. No connection could be demonstrated between it and a cavity above or with the gallbladder and its ducts. The calcareous lining of all three cavities was bile-stained. In the omentum and mesentery there were ten or twelve nodules varying in size from that of a pea to that of a walnut, and there was one cyst attached to the wall of a left inguinal hernia. Hooklets were demonstrated in them. A stone 1.5 cm. in diameter was found in the common bile duct, and a large cyst measuring 18 by 14 cm. was found in the right kidney. It contained many daughter cysts, scolices and hooklets, however, no hooklets or scolices were found in the cavities in the lung or below the diaphragm.

*Summary*—A German, aged 53, had a bronchobiliary fistula. There were multiple hydatid cysts in the omentum, mesentery and kidney. Discovery of scolices and hooklets proved them to be hydatid cysts. There was no direct proof that the cavities in the liver, subphrenic space and the right lower lobe of the lung resulted from hydatid cysts. It seems probable that the cavity in the lower lobe of the right lung was a secondary focus from rupture of the subphrenic cavity through the diaphragm.

BECK'S CASE <sup>69</sup> (1898)—An Austrian, aged 38, had been in the United States seven years. About six years before he had an attack of pleurisy with effusion. Serous fluid was aspirated from his chest. After slight improvement lasting about nine months, he was again taken sick. This time he coughed violently and expectorated much blood. He was then treated for consumption and admitted to a home for consumptives. About two years ago a slight swelling appeared under the angle of the right scapula, and in the course of about four weeks it became slightly painful. An incision revealed seropus and some improvement followed, but the cough accompanied by vomiting persisted as before. At last the expectoration became fetid, and the house physician, while searching for tubercle bacilli, detected hooklets and fragments of a cyst wall. A diagnosis of gangrene of the right lung was made, caused by invasion with the echinococci, and the patient was transferred to St. Mark's Hospital for operation. He was first seen by Dr. Beck on Nov. 22, 1897. Examination revealed a tall, emaciated man with a flat thorax which expanded symmetrically. The left lung was normal, but on the right side, anteriorly and below, there were tympanic sounds and also râles during inspiration. Posteriorly and below, there was slight dulness. Correspondingly, bronchial breathing and râles were heard. The heart was normal. The pulse rate was 106, the temperature 100.5 F. The patient suffered intensely under vehement coughing spells, especially in the morning, which were always followed by expectoration of a most offensive odor. Sometimes there was dyspnea and also hemoptysis. The sputum amounted to about 200 cc. in twenty-four hours and contained an abundance of pus, also fibers of the characteristic alveolar type, pigment, hematoidin crystals, disintegrated blood corpuscles, phosphate crystals, streptococci and leptothrix. No tubercle bacilli, hooklets or cyst fragments were found. When the patient expectorated little, the dulness was not pronounced, and the respiratory sounds were less audible than in the morning after copious expectoration. On November 24, pneumotomy was performed, chloroform anesthesia being used. An incision reaching from the midaxillary line to the transverse process of the sixth dorsal vertebra was made. The fifth, sixth and seventh ribs were resected. After a portion of the soft tissues, also the costal pleura, was removed, the lung

<sup>69</sup> Beck, Carl. Echinococcus of the Lungs, J. A. M. A. 31:1238 (Nov. 19) 1898.

collapsed slightly but soon assumed its former expansion. The edges of the cavity being well protected with sterile gauze, a strong aspirating needle was pushed forward into the center of the exposed area which yielded only blood. After various attempts in this direction were made in vain, the stilet tip of the Paquelin cautery was introduced carefully into the center of the exposed area. After a little over 1 inch of the lung tissue had been perforated, a stream of rust-colored pus of a most offensive odor escaped with a loud noise, and at the same time the patient collapsed. A sponge was quickly forced into the opening, and under artificial respiration and energetic stimulation, the patient rallied. On the following day the cavity was carefully washed, and much pus and detritus were discharged. The drainage was copious during the next four weeks, but repeated microscopic examinations revealed nothing extraordinary. During the first week after operation, the temperature varied between 99 and 101 F, while the pulse ranged from 90 to 100. The patient slept but little, and was tortured by coughing spells. As it seemed that there was some retention, probably due to the irregularity of the draining canal, Dr. Beck introduced a finger into the cavity, dilating it thoroughly. There was a discharge of a large amount of bloody pus, and by violent coughing, a thick membrane, rolled together like a cigaret was expelled. This proved to be a piece of a cyst wall. The patient now improved steadily, and the discharge lost its odor and became much less. The tube was discarded on February 6, and the wound was healed on February 21. He was discharged cured on July 20, 1898.

*Summary*—An Austrian, aged 38, had an attack of pleurisy six years before admission to the hospital, with cough and hemoptysis. He was treated for tuberculosis. Hooklets were discovered in the sputum. Suppuration of the cyst ensued. Recovery followed pneumotomy and removal of the wall of the cyst.

CHOWN'S CASE<sup>70</sup> (1901)—A man, aged 56, an Iclander, had lived in Winnipeg and Manitoba. There was a long period of expectoration and collapsed daughter cysts were expectorated for months.

*Summary*—The report of this case is not available in the literature except in this brief form in Lyon's report.

GAY'S CASE<sup>71</sup> (1901)—Angelo, T., a barber, aged 25, born in Italy, had been in America four years. He was first seen on Jan 10, 1901. He was always ailing up to his fourteenth year, with coughing, fever and general weakness. He was then fairly well until he was 23, when he was operated on in the Boston City Hospital for "dropsy." The scar showed that he had had a median laparotomy. He gave a history of slight attacks of hemoptysis and more or less pain constantly in the dorsal region. About Dec 1, 1900, he became quite ill, had much cough with blood-streaked expectoration, was weak, and had anorexia, marked debility, chills and fever, and pain in the lower right side of the chest. Physical examination showed much prostration, and moderate emaciation. There was a dusky pallor of the face. The temperature was 100.8 F, the pulse rate 98 and respiratory rate 30. There were diminished respiration and crepitant and subcrepitant râles with slight dulness at the base of the right lung. Small mucous râles and crackling were present at both apices. There was sinking in of the supraclavicular spaces. The patient apparently then had pneumonia of the right lower lobe, but recovered.

<sup>70</sup> Chown, H. H. Case Report, personal communication of Lyon's from Chown, 1901.

<sup>71</sup> Gay, W. F. Echinococcus of Liver with Perforation Into the Lungs and Bronchi, Boston M & S J 144 492, 1901.

by the end of January, 1901, so as to be up and about. The lower part of the right lung cleared leaving the other portions as before. At this time the liver was found to be painful and gradually enlarging. On March 1, he had several attacks of hemoptysis with much cough. Hemorrhage ceased in a few days, and the sputum became viscid and white. The lung showed a multiplicity of rales of all kinds. He was thought to have pulmonary tuberculosis. The liver showed uniform enlargement. Abdominal tympanites was present. He had fever, and much pain on coughing. The feces were clay-colored, fetid and pasty. There was no jaundice. There was a peculiar pallor which could be called dusky. He had an anxious expression, with pinched features and cold sweats. The symptoms continued for about one week, and on March 13 had reached the maximum. On March 14, he had several vomiting spells, the matter ejected being bright yellow, suggesting bile. The expectoration became more copious and a bright orange, and in a few days the temperature declined to 99 F. The breathing became less labored. The liver was soft and decreasing in size, and the general condition slowly improved. A diagnosis of perforation from the liver into the lungs and bronchial tube was made, but the underlying pathologic process was not understood until a small fragment of white hyaline material was found in the sputum suggesting hydatid. A search of the sputum daily soon revealed an entire cyst about the size of a pigeon's egg. The expectoration of cysts then became more common and from one to ten a day, ranging in size from that of a pea to that of a pigeon's egg, were expectorated. The material was examined by Dr F B Mallory, pathologist at the Boston City Hospital, who found the characteristic laminated membrane, daughter cysts and scolices. The orange color was due to crystals of hematoïdin. On April 10, the patient was said to be improving, the expectoration and dark orange color had disappeared. The temperature remained 99 F and pulse rate from 110 to 120. "This strain on the heart together with the general phthisical consolidation of the lungs will probably prove the fatal factors in the case."

*Summary*—An Italian, aged 35, had been in America four years. The case was reported by the author as one of "echinococcus of liver with perforation into the lungs and bronchi." A study of this case report suggests multiple infestations involving the lungs and the liver.

*STONE'S CASE*<sup>72</sup> (1903)—An Armenian who had been in the United States seven years, for ten weeks had had progressive loss of strength and weight. He suffered with pain in the epigastrium. After two weeks of suffering he had to stop work. There was fever, but no chills. For three weeks epigastric pain was very severe, and weakness and emaciation progressed rapidly. He was much emaciated and pale, and was sweating profusely. The sclerae showed a very slight yellow tinge. There was no leukocytosis. There was some bile in the urine. The heart was normal except for weak sounds. The left lung was normal. The lower right side of the chest was bulging. There was flatness from the fourth rib in front to four fingerbreadths below the costal margin. Below the fourth interspace in front and the midscapular line in the back, there was absence of fremitus and respiratory murmur. Below the ribs, extending nearly to the midline was a convex bulging tumor. On respiration, there was a palpable crepitus and a loud friction rub over the outer part of the tumor. There was doubtful fluctuation over the tumor. The right side of the back showed dullness at 2 inches

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<sup>72</sup> Stone, A K. Echinococcus Cyst of the Liver and Lungs, Boston M & S J 149 263, 1903

below the angle of the scapula quickly becoming flat. Respiration and tremitus were diminished and lost below the angle of the scapula. Above the dulness respiration was harsh but of diminished intensity.

Operation was performed by Dr. C. B. Porter. An incision was made parallel to the costal margin over the tumor. At a depth of 2 inches in the liver a cyst was found containing about 4 parts of purulent material. There were many daughter cysts varying in size from that of a pea to 2 inches in diameter. The cavity was packed with gauze because of hemorrhage. The patient died rather suddenly on the fourth day.

Autopsy on Dec. 13, 1902, showed the liver to be about normal in size. In the right lobe there was a large irregular cavity probably 15 cm. in diameter with a rough, irregular lining composed chiefly of a patchy layer from 2 to 3 mm. thick, of a dirty greenish-gray, somewhat friable granular material. Adherent to this in places were plaques and patches of dense but friable dirty grayish

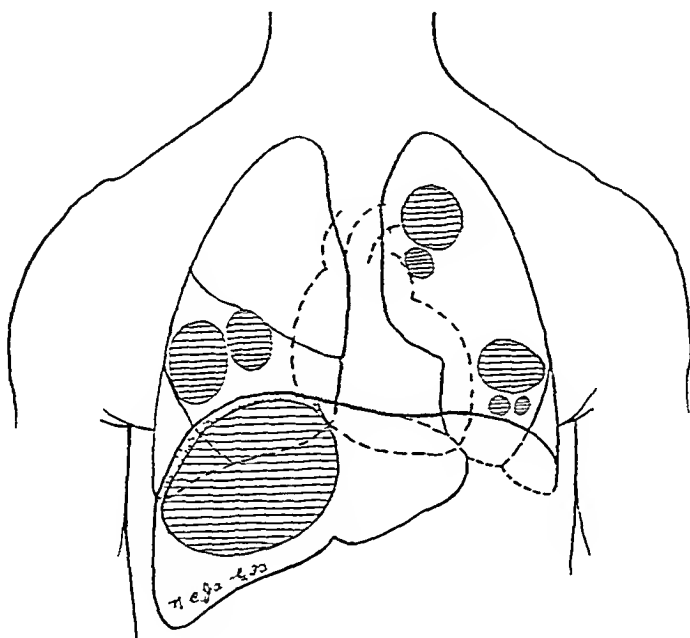


Fig. 15 (Stone's case).—Multiple cysts in both lungs and the liver.

opaque, tough substance from 2 to 3 mm. thick and not easily removed from the lining of the cavity. In places the lining resembled mucous membrane of the gall ducts, and these areas are apparently continuous with the hepatic ducts. The diaphragm was adherent to the liver and formed probably a part of the wall of the cavity. The lining of the cavity seemed to be separated from the liver substance by a thin layer of connective tissue.

In each lung cystic structures were found in the midst of the pulmonary tissue which bulged outwardly beneath the pleura. Where they bulged the most they had a grayish translucent wall apparently formed by little more than the pleura. In the median lobe of the right lung there was a cystic structure 3 cm. in diameter. In the lower lobe of this lung there was a cyst 7 cm. in diameter. The upper lobe of the left lung contained a cyst 4.5 cm. and near this there was a collapsed cystic structure 3 cm. in diameter. The lower lobe of the left lung showed a multilocular cystic structure 6 cm. in diameter and also two cysts 1.5 and 1 cm. in diameter. These were filled with a clear fluid and possessed a

white gelatinous lining 1 mm thick. This was readily removable, leaving a smooth surface apparently formed by a mass of connective tissue. Sections of the wall of the cysts in the left lung showed a chitinous layer with brood capsules containing scolices.

*Summary*—An Armenian, who had been in the United States seven years, presented no pulmonary symptoms. He was operated on for a large cyst of the liver and died on the fourth day after operation. Seven pulmonary cysts scattered throughout the lungs except the right upper lobe were found at autopsy. Scolices were found upon microscopic examination (fig 15).

**GURLEE'S CASE**<sup>22</sup> (1905)—Lizzie P., aged 27, a native of Italy, came to the United States in 1904. She was admitted to the Cook County Hospital on April 2, 1905. She had a cough for four months, pain in the chest and abundant expectoration,

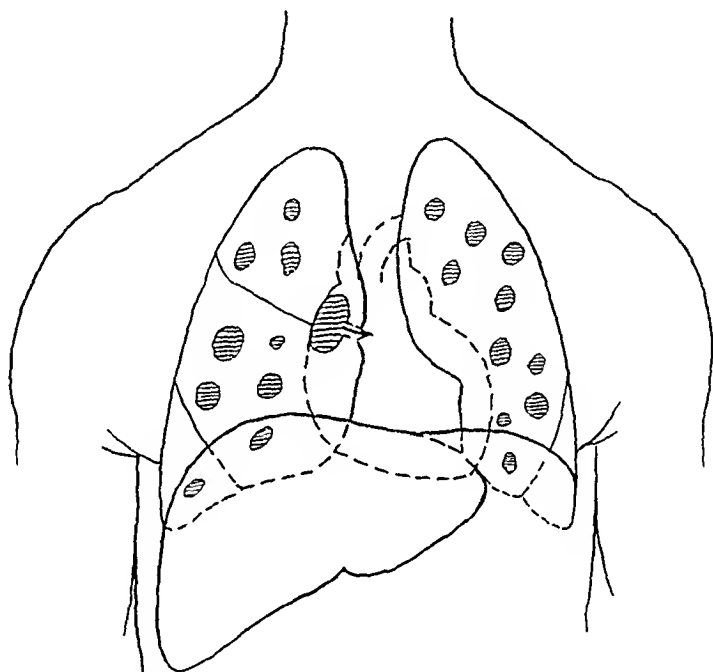


Fig 16 (Gurlee's case)—Cyst of the right auricle rupturing into the blood stream with secondary sowing of each lung.

tation, which at times had been bloody. She had had nausea and vomiting and had lost 40 pounds (18.1 Kg).

Examination revealed an emaciated woman who could not speak above a whisper. There was dulness from the right border of the sternum to three-fourths inch beyond the left nipple. There was a long, loud, rough, systolic murmur at the apex and a loud systolic murmur over the pulmonic area.

Dulness existed anteriorly and posteriorly over the upper lobe of the right lung, and there was some dulness posteriorly over the upper lobe of the left lung. Low down posteriorly just to the right of the vertebral column there was an area about the size of the palm with somewhat tympanic percussion. Moist râles and bronchial breathing were heard over the right upper lobe and a few mucous râles over the middle lobe. There was bronchial breathing over the apex of the left lung with a few moist râles in the left axilla. A diagnosis of pulmonary tuberculosis was made and confirmed by examination of the sputum. The cough was violent, and there was a large quantity of purulent sputum. There was

extreme dyspnea. On April 5 she coughed up a small cyst about 1 cm in diameter which was ruptured and showed what seemed to be a subcut. The fluid of this cyst failed to show in hooklets but a large number of small round bodies found within which the echinococcus embryos could be seen. The walls of the cyst were laminated. Several examinations of the sputum were negative for hooklets. The blood showed no eosinophils. The patient died suddenly on April 10.

Postmortem examination showed no fluid in the pleural cavity. The apex of the right lung was adherent to the pleural wall. Through it both lungs could be palpated rounded masses corresponding to the echinocyst. The left lung crepitated throughout the right upper lobe was almost solid and in the middle and lower lobes could be felt hard stolidic masses irregular in outline. On section the left lung showed several large cysts throughout both lobes varying in size from that of a pea to that of a lens. The right lung showed practically the same distribution of echinocystic cysts; the number may have been slightly greater. Disseminated tubercles were found in the middle and lower lobe of the right lung. A large cyst in the upper portion of the right lower lobe was removed without rupture. The fluid contained many proliferous vesicles in which the characteristic echinococcus embryos could be seen. The wall had the characteristic laminated appearance and on its inner surface were seen numerous daughter cysts. Some of the cysts in the right lung were infected. The central portions of the lungs were nearly free from cysts. The cysts occurred mostly at the periphery of the lung.

A cyst about the size of a pin's head was found in the posterior wall of the right auricle. It had ruptured internally and a blood clot adhered to the endocardial opening. When this clot was removed several daughter cysts varying in size from that of a pinhead to that of a pea escaped. The muscles of the heart had undergone no appreciable change, and there was a thin layer of fibrous tissue between it and the cyst. There were no cysts in other organs. Dr Gurlee concluded that this case represented a primary cyst of the heart with secondary infection of the lungs.

**Summary**—A woman, aged 27, a native of Italy, who had been in the United States about one year, had multiple cysts throughout both lungs, probably originating from a cyst in the right auricle which had ruptured into the blood stream (fig. 16).

**SIXTH CASE** (1905)—A man, born in Greece, came to the United States about five years before examination. Six years previously he complained of acute sharp pain, which he referred to the left side and upper segment of the lung. Since then he had had occasional difficulty in breathing and attacks of coughing. His general condition on admission was fair. There was a distinct, well defined diffuse area of dullness over the left side and the upper part of the lung. The breath sounds were feeble on the left side, with bronchial breathing in the area of dullness. Aspiration was attempted in the center of the dull area, with negative results. On the night of the day on which aspiration was performed, the patient had a violent attack of coughing and raised  $1\frac{1}{2}$  pints or 1 quart of fluid. On microscopic examination, echinococcus hooklets and scolices were found. The rupture of the cyst was followed by a violent reaction, from which he gradually recovered. Expectoration became less and less, and instead of dullness there was resonance on percussion. A number of days after the spontaneous rupture of the cyst there was vesicular breathing.

*Summary*—A man, a native of Greece, with symptoms of six years' duration had pain, cough and difficulty in breathing. There was spontaneous rupture of the cyst in the left lung into the bronchial tree following a negative aspiration. Hooklets and scolices were found in the sputum.

**GARRETT'S CASE**<sup>74</sup> (1906)—L. S., a colored woman, aged 46, a native of Worcester County, Maryland, was admitted to the State Asylum on Feb. 19, 1889, for treatment for manic-depressive psychosis. Her general health was excellent for twelve years, when attacks of syncope developed which were followed by more or less stupor lasting several days. These attacks were evidently nephritic, as the urine contained hyaline and granular casts in abundance. There was marked arteriosclerosis. She soon improved, and remained in fairly good health until the final illness. On April 16, 1906, after a few days of apparent malaise and indisposition, she began to have a mild diarrhea accompanied by nausea, vomiting and slight fever. On May 2, she had "a chill followed by fever of 104 F." At this time cough was first noted.

Physical examination revealed dulness over a limited area of the right middle lobe, posteriorly, with coarse rales. A septic temperature persisted. There was rapid loss of weight. The sputum was swallowed, and only once could it be examined. No tubercle bacilli were found, but elastic tissue was present. She died on May 27, of what was thought to be pulmonary tuberculosis.

Autopsy showed a cavity the size of a hen's egg in the upper portion of the middle lobe of the right lung, posteriorly. It was surrounded by a thick wall, and contained dark brown fluid not unlike thin, dirty pus. The cavity communicated with a bronchus. The cyst contained the same layers as described in the cyst of the liver. In the center of the right lobe of the liver there was a cyst about the size of a fist. It contained yellowish, granular semisolid, caseous material resembling curd. The walls of the cyst were thick, sharply defined and easily separated into two distinct layers, the inner one being thicker, grayish and friable. The outer layer was thinner, darker and much tougher. Hooklets were found in each cyst. No scolices were demonstrated.

*Summary*—A woman, aged 46, native born, an inmate of the state asylum for about seventeen years, had a hydatid cyst of the right middle lobe which ruptured into a bronchus. It was infected. A quiescent cyst was found in the liver. The diagnosis was made at autopsy. Hooklets were found.

**SMITH AND HARRINGTON'S CASE**<sup>75</sup> (1907)—Alexander Auchals, aged 23, was born and had always lived in southern Russia. About six weeks before entrance to the hospital, on Dec. 12, 1906, he had left home and sailed for America. At that time he felt well. On the ninth day of his journey, he began to have pain in the right side of the chest, which had been fairly constant since then. The pain had no relation to deep breathing, cough, position or food. There was no cough or sputum. On admission to the hospital, the whole right side of the chest was flat throughout. The heart was  $1\frac{1}{4}$  inches outside the left nipple line. The liver dulness was 2 inches below the costal margin. The interspaces in the right side of the chest were noticeably obliterated. There was bronchial breathing with a suggestion of amphoric note with bronchophony over the right side of the chest. Aspiration was performed on this side just below the angle of the scapula, with

<sup>74</sup> Garrett, R. E. Hydatid Cysts with a Report of a Case, Maryland M. J. 49:373, 1906.

<sup>75</sup> Smith, W. H., and Harrington, F. B. A Case of Echinococcus Cyst of Lung and Abdomen. Boston M. & S. J. 156:180, 1907.

negative results. Aspiration was again performed in the posterior axillary line where there was absolute flaccidity and thin turbid purulent fluid was obtained which did not flow readily. A little more than 1 pint was withdrawn. There were no clots in the sediment which was composed of pus cells. No clots were found but subsequently after repeated coughing they were demonstrated. Subsequently he was tapped in the posterior axillary line and 1 pint of similar fluid was withdrawn each time. The patient did not do well. He had some pain in his side and there was a rise in temperature to 101 F. Operation was performed on December 19. A portion of the eighth rib was removed and the pleural cavity opened. There was a definite several pints of fluid containing cysts in large number. A few large intercostal cysts were found filling the pleural space and pressing on the bladder.

**Summary.**—A male aged 25 born in the United States was sent to a rural area of the United States. He came to the attention of the physician on the right side of the chest. There was no cough or expectoration. There were physical signs of fluid in the right pleural cavity. Turbid yellow fluid was aspirated from the right side of the chest on three occasions. Thoracotomy was performed by removal of a section of the eighth rib. Several pints of fluid containing a large number of cysts was evacuated. Clots were found in the pleural fluid. This case is recorded in the literature as a case of echinococcosis of the lung and abdomen. It is more likely a case of pleural cyst.

**MacDONALD'S CASE 7 (1913).**—A male aged 18 a native of New Zealand was admitted to St. Joseph's Hospital San Francisco on May 22, 1912, complaining of cough, weakness and burning of breath and expectoration of pus and pain in the left side of the thorax for a time. Two and a half years before admission he had lived in one of the notorious hydatid areas in New Zealand.

Examination revealed the apex of the heart about 1½ inches to the right of the sternum. The left side of the thorax gave a complete typical picture of hydropneumothorax. Operation was performed on May 5, 1912, with the patient under ether anesthesia. Incision of 2 inches on the seventh, eighth and ninth ribs in the midaxillary line was done. A considerable amount of seropurulent fluid and a large number of collapsed and dead hydatid cysts together with two large normal ones were obtained. The total amount of fluid and cysts measured 3 quarts. A second operation was performed on June 10 when a portion of the tenth rib close to the spine was resected to give better drainage. There was a bronchopleural fistula. He was discharged on September 17. He still had two drainage tubes in the pleural cavity which held about 3 ounces and communicated with a bronchus. He was last heard from by letter on November 17 when he reported that he was much improved, and that his back was nearly healed.

**Summary.**—A youth aged 18 a native of New Zealand had a cough, purulent expectoration, and pain in the side. The picture was that of hydropneumothorax. Three quarts of purulent fluid and hydatid cysts was obtained from the left side of the chest by thoracotomy. The patient was well on his way to recovery when last heard from. This case probably represents a pulmonary hydatid cyst rupturing into the pleura and into a bronchus, such as has been described by Dene.

**RAMEY AND EMERSON'S CASE 77 (1915).**—A Greek, age not given, about one month before coming under observation had been in a hospital for one week

76 MacDonald, G. C. Hydatid Cyst of Left Lung, *Pacific M. J.* 56:271, 1913.

77 Ramey and Emerson. Echinococcus Disease. Report of a Case, *West M. Rev.* 20:171, 1915.



and had been treated for pneumonia. Following this he coughed a great deal and did not regain strength. The history was unsatisfactory, because he could not speak English. Physical examination revealed absolute dullness over the lower posterior area of the right side of the chest. The breath sounds were absent. A soft, tense tumor, transmitting a peculiar thrill on percussion, was present in the right epigastric region, apparently closely associated with the liver. The palpable portion of the tumor was as large as an orange. Frequent examinations of the sputum were negative for hydatid elements. Exploratory aspiration of the chest revealed a spurt of reddish-yellow fluid, then sudden complete stoppage of the flow. Examination of this fluid did not show hooklets or other evidence of echinococcus disease. The patient rapidly became emaciated, and had an irregular temperature. Operation consisted of the resection of three ribs. There escaped from the wound about 2 quarts of yellow pus tinged with red and about 200 cysts of all sizes, from that of a pinhead to that of an orange. All of the cysts were brown, collapsed and dead. In the subsequent drainage, other cysts appeared from time to time. About one month later, a large cyst of the liver was treated by operation. Drainage from the wound in the chest persisted for several months. It finally healed, but after a period of two or three months broke open and discharged. He then had a cough, lost flesh and expectorated two or three collapsed brown cysts. The patient disappeared from observation. Scolices and hooklets were recovered in the fluid from the cyst of the liver.

*Summary*—A Greek, age not known, had a cough. A cyst with daughter cyst formation was found in the right pleural cavity, probably originating in the lung. It was complicated by a hydatid cyst of the liver. He was improved by operation, but disappeared from observation while drainage still persisted from the right side of the chest.

DAVIS AND BALBONI'S CASE<sup>78</sup> (1917)—A man, aged 27, an Italian fruit pedler, had been in this country fifteen years. He was admitted to the Massachusetts General Hospital on Aug. 23, 1912 (service of R. I. Lee). In 1910, he had had a severe attack of pain in the epigastric region. At this time he first noticed a small swelling below the ensiform appendix. Similar attacks at irregular intervals had persisted. After two years the swelling had increased perceptibly. Examination revealed just below the ensiform appendix a prominence which moved with the liver on respiration. It was smooth, doughy and tender. The mass apparently sprang from the left side of the liver. The right side of the chest was dull from the inferior angle of the scapula down, and an occasional dry crackle was heard. Roentgen examination gave negative results. The Wassermann reaction was negative. The white blood count was 5,200, eosinophils 1 per cent and hemoglobin 80 per cent. The coagulation time was seven minutes. A diagnosis of echinococcus disease of the liver was made and operation suggested. The patient refused to remain in the hospital longer than one week. On Jan. 22, 1915, he was operated on by Dr. R. P. Bonelli in a private hospital. A huge cyst of the liver was removed at operation. Scolices were found. On January 26 and February 10, the echinococcus-fixation test gave strongly positive results. He was discharged in good condition on February 13. The sinus on the right seemed to communicate with the chest cavity, for when the patient coughed there was an expulsion of air through the sinus. During the rest of February and March the patient had a dry cough and evening fever. The sputum was negative for tubercle bacilli.

<sup>78</sup> Davis, L., and Balboni, G. M. A Study of Twenty-Nine Cases of Echinococcus Disease, Boston M. & S. J. **176**: 826, 1917.

Examination showed consolidation of the medial and anterior lobes. He expectorated large quantities of mucus, sometimes bright red and at other times of pink juice appearance. Hooklets were present in the sputum. The cough and expectoration decreased and disappeared in June. The sinus was completely healed in May. The echinococcus fixation test was negative on December 7. At the time this case was reported, May 24, 1917, the patient was well and working.

*Summary*—A man, aged 27, an Italian had been in this country fifteen years. A hydatid cyst of the liver was cured by operation. It was complicated by a hydatid cyst in the right lung which apparently cured itself by drainage into the bronchial tree. Hooklets were found in the sputum.

CLARKSON'S CASE 77 (1917)—A Macedonian youth, aged 18, was admitted to the hospital on April 14, 1912, complaining of pain, cough and shortness of breath, which began with a chill two weeks prior to admission. Respiration was 46, temperature 101 F and pulse rate 100. In the left lung there was a rounded and circumscribed area of dullness extending from the second to the sixth rib and from the mammillary line in front to the anterior angle of the scapula behind. The breath sounds were distant and the vocal resonance much diminished in this locality. The rounded area of dullness and the shape of the shadow on the roentgenogram suggested a cyst. On aspiration 510 cc. of clear, limpid fluid was obtained which on examination showed slight traces of albumin and many heads and hooklets of the echinococcus. The white blood cells numbered 23,000 with no increase in the eosinophils. Operation was performed and a large cyst of about 12 ounce capacity was rather easily removed. It contained many daughter cysts. The recovery was slow and tedious, a sinus persisting for a long time.

*Summary*—A Macedonian youth, aged 18, suffered from pain, cough and shortness of breath. The diagnosis was made by an exploratory aspiration. The cyst was removed at operation, and recovery slowly followed.

CLARKSON'S CASE 271 (1917)—An Italian, aged 25, a laborer, was admitted to the Toronto General Hospital on June 15, 1914, complaining of severe pain on the left side, which was increased on coughing. The onset was sudden, accompanied by a chill. The temperature was 102 F and respiratory rate 30, the sputum was bloody. The left side of the chest was decidedly limited in its movements. Posteriorly, there was an area of absolute dullness above this relative dullness as high as the fifth rib. The heart was slightly displaced toward the right. Fluoroscopic examination showed the diaphragm on the left side to be 8 cm. below the nipple, immovable but arched. The costophrenic angle was clear. In the middle portion of the left lung toward the base was a large rounded shadow which did not move on respiration. On exploratory aspiration, 25 cc. of clear fluid under slight pressure was obtained. This was of low specific gravity and contained a slight trace of albumin but no hooklets. The patient's general condition improved, and he was discharged from the hospital and lost from observation until April 6, 1915, when he was admitted to the Western Hospital suffering from a troublesome cough with abundant sputum. He also had a severe pain in the left side. The temperature was 102.4 F, pulse rate 100 and the respiratory rate 28. The left side of the chest showed restricted movements, and vocal fremitus was absent over the lower quadrant. There was absolute dullness below the seventh rib anteriorly. Posteriorly, beginning at the level of the seventh dorsal spine, there was relative dullness. In the lower part of the chest there was absolute flatness. Over the dull area, the breath sounds were absent. Exploratory puncture in the ninth space,

posterior axillary line, yielded 1 cc of fecal-smelling pus in which staphylococci and bacilli were found. The white blood cells numbered 9,000, with few eosinophils. Operation was performed on May 6. A portion of the ninth rib was resected in the posterior axillary line. At some distance from the surface was found a cyst full of foul-smelling pus, the walls of which were thin and gelatinous in structure and came away by piecemeal. No daughter cysts were obtained. The patient tolerated the operation poorly. He coughed up large quantities of the cyst wall and quantities of blood. After a rather slow convalescence, he made a good recovery.

*Summary*—An Italian, aged 25, a laborer, presented the symptoms of pain in the left side, cough and hemoptysis. The onset was acute. The diagnosis was made by roentgen examination and aspiration on the first admission to the hospital, but he was discharged and disappeared from observation for nearly a year, when he returned with a suppurating cyst which was cured by operation.

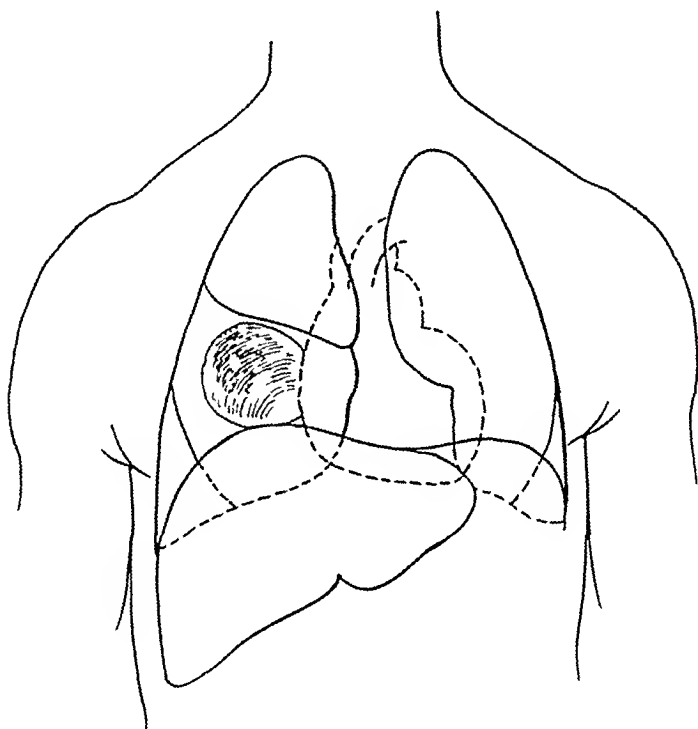


Fig 17 (Crow's case)—Large solitary cyst in the right middle lobe

CROW'S CASE<sup>80</sup> (1918)—A farmer, aged 30, a native of Spain, was first seen in November, 1917. His present trouble began five years before admission, with intermittent pains in the upper part of the back. Six months later he began having gastric distress and indigestion. The results of the physical examination were negative. The patient was referred to the x-ray laboratory for examination of the gastro-intestinal tract. A roentgenogram revealed a cyst in the lower right side of the chest, 12 by 10 cm. Operation was performed on November 18, with the patient under nitrous oxide anesthesia. A trap door incision was made in the anterior right side of the chest over the third, fourth and fifth ribs. When the pleura was opened, the lung was collapsed, and embedded in its tissue was seen the white, glistening, mother-of-pearl-like surface of the cyst. The cyst was attached to the pericardium and pleura. The inner layer of the cyst was dissected away.

<sup>80</sup> Crow L. B. Echinococcus Disease of the Lungs, *Am J Roentgenol* 5: 513, 1918.

from the outer fibrous liver and when freed, luted through the opening where it unfortunately burst and allowed the contents to spill in the chest cavity. The cavity was well sponged. An attempt was made to remove some of the outer fibrous liver, but the slightest traction on the lung caused immediate cessation of respiration so that this attempt was given up. The cavity was packed with gauze dipped in 10 per cent formaldehyde glycerin solution. The wound was closed. The immediate postoperative convalescence was very stormy. After a few days the lung began to expand. For two weeks the patient had a septic temperature. Three days after operation he had a profuse expectoration of brownish mucopurulent pus accompanied by severe attacks of coughing. He gradually improved so that at the time of this case report he had recovered and was soon to leave the hospital as cured.

**Summary**—A Spaniard, aged 30, presented no pulmonary symptoms other than pain in the back of five years' duration. The diagnosis was made from roentgen examination. Cure was apparently obtained by pneumotomy. No report of the microscopic examination was given (fig. 17).

**GLASSMAN'S CASE<sup>81</sup> (1922)**—A woman, aged 30, a Siberian, was admitted to the hospital on Jan. 6, 1922. For eight months she had had belching, nausea and vomiting after meals. A dull more or less continuous pain later developed in the right side of the abdomen. There was a mass in the right hypochondriac region which was smooth and tender. It moved with respiration. The clinical diagnosis was hydrops of the gallbladder. Roentgen examination showed a mass in the right hypochondriac region, and the roentgen diagnosis was cyst of the liver. Operation was performed on January 17 when three cysts of the liver were found. The largest was about the size of a grapefruit. Two cysts were removed, one was packed with gauze. The patient died on January 18. Postmortem examination revealed two cysts in the right lower lobe of the lung and one cyst in the left upper lobe. The cysts occupied about two thirds of the lung. There were no pulmonary symptoms and no roentgen examination of the chest had been made.

**Summary**—A Siberian woman, aged 30, died following operation for multiple cysts of the liver. At autopsy, two cysts were found in the right lower lobe and one cyst in the left upper lobe.

**BABONIS CASE<sup>82</sup> (1922)**—A A., aged 22, a Greek, a farm hand, had been in the United States five years. He was admitted to the outpatient department of the Massachusetts General Hospital on Feb. 17, 1917. His chief complaints were cough, pain in the chest and blood in the sputum. He had had a cough for two years. One and a half years before admission, after slight exertion, he coughed up a teaspoonful of bright red blood. About one year before he coughed up one glassful of bright red blood. He remained in bed for three months, and had bloody sputum daily in streaks and clots. He then resumed work, but every three or four weeks had a little bloody sputum. One month before examination he coughed up one teaspoonful of blood. During the past one and a half years the cough had been slight, mostly in the morning. He raised two or three teaspoonfuls of sputum during the course of the day. He felt well and was able to work without feeling tired. He had a good appetite, but had lost some weight. He had had no night sweats. Three or four days before admission he felt tired and was unable to work. He had a true chill late the next evening and felt feverish. He also had some pain in the anterior right side of the chest on coughing.

<sup>81</sup> Glassman, J. Radiological Findings in a Case of Echinococcus Cyst of the Lung and the Liver, *M. J. & Rec.* **119**: 144, 1924.

The chest was well developed, and expansion was equal. There was dulness at the base of the right lung posteriorly and anteriorly, with diminished breath sounds and whispered voice from about one fingerbreadth from the angle of the scapula downward. The abdomen was slightly tender over the liver, which was palpable. The sputum was negative. The blood smear was normal. The Wassermann reaction was negative. The echinococcus fixation was negative. Roentgen examination (by Dr G W Holmes) showed a round tumor mass at the base of the right lung, about the size of a grapefruit. The lower border was mostly below the dome of the diaphragm. This shadow did not move with ordinary respiration, but could be displaced somewhat with forced respiration. It was of even density throughout, and its borders were sharply defined.

Thoracotomy was performed (by Dr W Whittemore). The right seventh and eighth ribs were resected below the angle of the scapula. The pleura was somewhat thick, and there were many fine adhesions between the pleura, and a firm

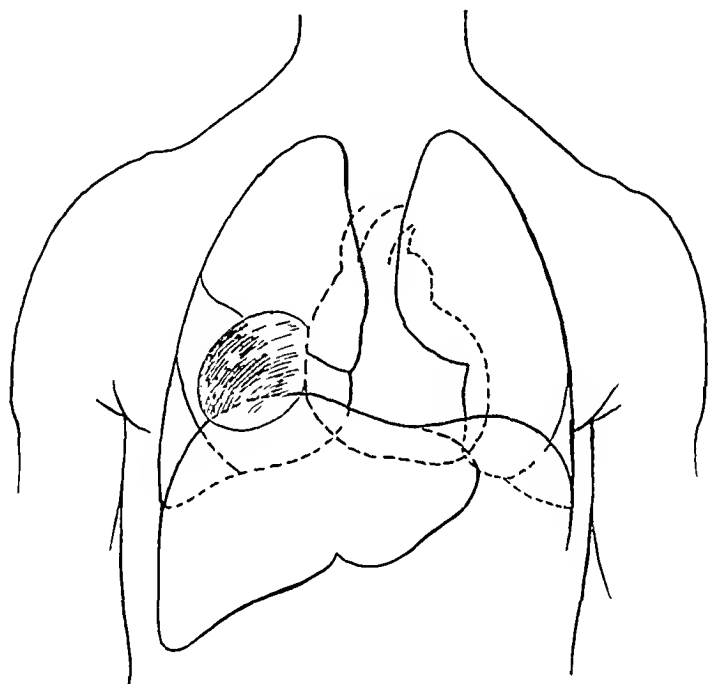


Fig 18 (Balboni's case 1) —Large solitary cyst in the right lower lobe

mass in the right lower lobe. The mass was sutured to the pleura, and an incision about 1 inch deep into the mass seemed to go through lung tissue. A needle was inserted  $\frac{1}{4}$  inch further, and a small amount of clear fluid found. The patient began to expectorate clear fluid through the nose and the mouth. Finger dissection into the mass opened a large cyst filled with clear fluid. About 1,500 cc of clear fluid was evacuated. No small cysts or hooklets were found. A cigaret drain was introduced into the cavity.

According to the pathologic report, there was chronic inflammation, but no evidence of echinococcus. The patient was discharged on Jan 6, 1918. The wound was clean and solidly healed. He was readmitted to the hospital on Sept 19, 1919, and gave the following history. Since leaving the hospital he had had a persistent cough, especially in the early morning and at night. He had still raised a small amount of blood, sometimes bright but usually dark. He had had no large hemorrhage. There had been dull pain in the lower right side of the chest. He had been working on a farm up to ten months previously, when the pain became too severe for him to continue work. He had not lost weight, but felt weak.

Examination of the thorax showed some limitation of motion of the base of the right lung. There was dullness from the seventh rib down on the right side of the back extending in the front to the fifth rib. There were absent tactile fremitus, diminished to absent whispered voice, vocal fremitus and breath sounds in the area of impaired resonance. On September 24, with the patient under gas-oxygen anesthesia thoracotomy was performed by rib resection (Dr. Whittemore). The lung was adherent to the costal pleura. A large tumor mass presented in the lung. On opening into this, it proved to be a large cyst, and a considerable amount of clear fluid was evacuated. Several large fragments of cyst wall were removed. The cavity was picked with gauze and the wound closed. Packing was removed on the fourth day and on the following day the remainder of the cyst was expelled through the operative wound. In three weeks the incision was healed and the patient had an uneventful convalescence.

According to the pathologic report, irregular pieces of the wall of the cyst showed smooth, pearly white surfaces which had an elastic consistency. No hooklets could be found on fresh examination. Microscopic examination showed a laminated membrane without cellular structure. The gross and histologic appearance was in every way consistent with that of an echinococcus cyst.

**Summary**—A Greek, aged 22, who had been in the United States five years, had symptoms of cough and pain in the chest and blood in the sputum of from one and one-half to two years duration. The cyst was drained at the first operation, but the cyst wall was not removed. About twenty-one months later the cyst wall was removed at a secondary operation. Scoleces or hooklets were not discovered, but the cyst wall had the characteristic appearance of a hydatid cyst (fig. 18).

**BARTON'S CASE 2<sup>nd</sup> (1922)**—P. P. a Greek, aged 25, a laborer in a cotton mill, had lived in the United States for five years. He was admitted to the outpatient department of the Massachusetts General Hospital on Sept. 24, 1919. His chief complaints were pain in the chest and cough with blood in the sputum. About two years before admission he was hit on the right side by a piece of iron which fell on him. He was in a hospital in Youngstown, Ohio, for four months. At this time he began to cough a great deal, often raising bloody sputum. He felt fairly well after leaving the hospital, and the cough left him. About six months later, cough and hemoptysis returned, and the pain increased in the chest. He was unable to work for seven months. He sometimes had pain in the left side of the chest also. He was well until the onset of the present illness. He was a shepherd in Greece, and had dogs associated with him.

Physical examination showed a well developed chest, there was greater expansion on the left side than on the right. The heart was normal in size and position. The right side of the chest was dull below the spine of the scapula almost to flatness with rales and bronchial breathing. It was dull in the axilla. There were rales in the lower half of the left lung with some bronchial respiration. Examination of the blood showed white cells, 7,800, red cells, 7,396,000, hemoglobin, 100 per cent, polymorphonuclears, 78 per cent, eosinophils, 5 per cent, mass cells, 5 per cent, lymphocytes, 5.5 per cent, and large mononuclears, 11 per cent. The Wassermann reaction was negative. The reaction to the celunococcus-fixation test was strongly positive. The sputum was mucopurulent and was negative for hooklets, fragments of membrane or tubercle bacilli. Roentgen examination (by Dr. G. W. Holmes) showed an area of increased density 4 cm. in diameter in the left side of the chest below the fifth rib. It was round and of even density, with sharply defined borders. When the position of the tube was changed overlying it, there was a ringlike shadow of diminished density, which changed its relation

suggesting a different plane to the dense shadow. Neither shadow reached the periphery. A similar, slightly larger process was seen in the right lung below the fourth rib. On Feb 16, 1920, a roentgenogram made following oxygen inflation of the abdomen showed a distinct outline of the liver and the spleen. They appeared to be normal in size and shape. Just below the lower margin of the liver there was a round, dense mass, which was apparently connected by a band of adhesions to the anterior abdominal wall. There was a ringlike shadow in the left kidney, having all the appearance of an echinococcal cyst. The patient received nine roentgen treatments between Oct 3, 1919, and May 15, 1920, at from two to four week intervals. There was no improvement in the symptoms or change in the roentgen observations nor any change in the fixation test taken on three different occasions. When last seen in May, 1920, he still complained of an irritative cough, occasionally blood-streaked sputum and pain in both sides of the chest and in the region of the left kidney.

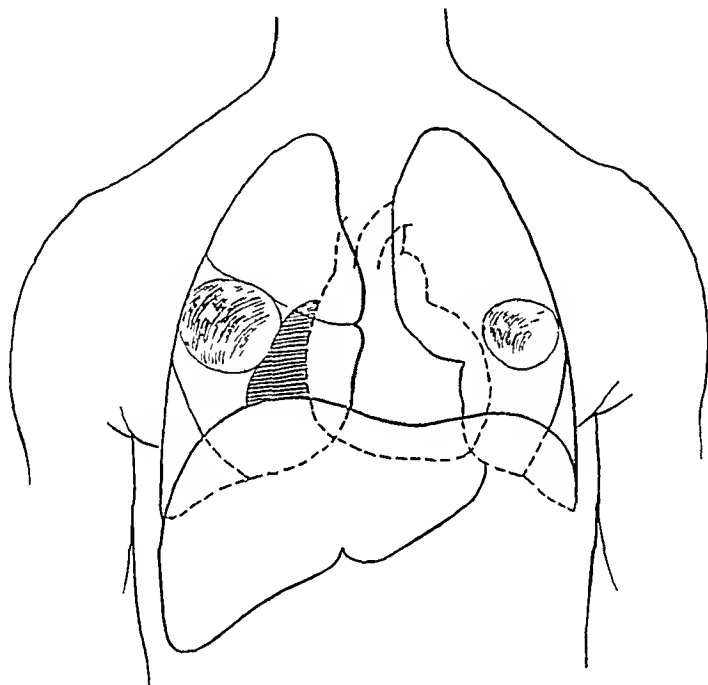


Fig 19 (Balbani's case 2) —Bilateral cysts

*Summary*—A Greek, aged 25, a shepherd while in Greece, had been in the United States five years. The symptoms presented were pain in the chest, cough and hemoptysis. The echinococcus-complement fixation test gave strongly positive results. There was roentgen evidence of hydatid cysts in the lower part of the lungs, and in the left kidney and an intraperitoneal cyst below the liver. There was no improvement following roentgen therapy (fig 19).

MILLS' CASE<sup>82</sup> (1922) (Case of Dr A F Wagner)—J G, a French woman, aged 36, was found dead. On Jan 21, 1922, postmortem examination showed a hydatid cyst of the right ventricle of the heart, 5 cm in diameter. It had the typical laminated cyst wall. There were no daughter cysts or scolices. In the substance on the inner side of the lower lobe of the right lung, there were four cysts the size of a walnut. The left lung was normal.

<sup>82</sup> Mills, H W. Hydatid Cysts of the Heart, with Report of a Case, *Surg Gynec Obst* **35** 455, 1922.

Pathologic examination (Dr. Brem and Dr. Zeiler) showed a rounded prominence about 4 cm. in diameter at the apex of the right ventricle. In the center of the ventricle the apical portion was narrowed by a mass lying in the apex and pushing upward and inward the surface of the intraventricular septum. Section of this mass showed an old cyst 5 by 4 cm. Attached to its wall was a crumpled folded membrane which was more or less translucent. The cardiac tissue covering the cyst was little more than the endocardium. The left ventricle was of normal size and was not invaded by the cyst. Microscopic examination of a section from the wall of the cyst showed an eosin-staining laminated membrane without nuclei and outside this a fibrous connective tissue capsule. About this was a zone of inflammation containing a few round cells and great numbers of eosinophils and lymphocytes. The diagnosis was echinococcus cyst of the heart.

*Summary*—A French woman aged 36 was found dead. At autopsy a hydatid cyst was found in the right ventricle and four cysts in the lower part of the right

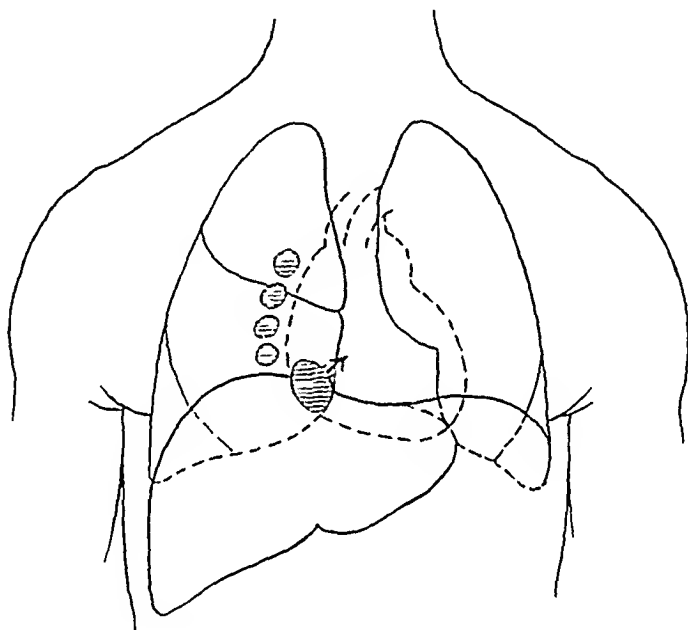


Fig. 20 (Mills' case)—Cyst in the wall of the right ventricle, multiple cysts in the right lung

lung. Dr. Wagner believed that the process started in the lungs and infected the heart by direct extension. Dr. Mills believed that the cyst of the heart was primary and the pulmonary cysts metastatic from it. As there was no evidence that the cyst in the right ventricle had ruptured into the blood stream, it is probable that the cysts of the lung and that of the heart had no immediate connection, all being the result of a primary infestation (fig. 20).

**CURRAN AND LOCKE'S CASE**<sup>55</sup> (1924)—A Syrian woman, aged 52, was admitted to the hospital on Dec. 12, 1918. She had been in the hospital on three previous occasions, first in 1909, when she was operated on for a large cyst of the liver containing innumerable daughter cysts. The second admission was four months later because of a discharging sinus. The third admission was in 1912, during which hospitalization she was operated on for recurrence of the hydatid cyst of the liver. Physical examination at the time of the present entry showed a well developed and well nourished woman lying in bed, with great dyspnea and pain



The chest was flat on the right side to the third rib posteriorly with absence of breath sounds. There was slight bulging of the interspaces over this area. The abdomen was greatly distended. There was a large, hard tumor on the right, extending from the costal margin to the crest of the ilium and to the navel in the midline. There was also a smaller mass hanging just below the ensiform appendix. Aspiration was performed on the right side of the chest through the eighth interspace in the midscapular line, and "a small amount of straw-colored fluid was withdrawn. The needle was passed in different directions and small cysts were apparently tapped with the withdrawal of a small amount of fluid from each one." Microscopic examination showed echinococcus remnants in the fluid. This patient died following laparotomy, at which time a large cavity containing a great quantity of purulent, foul-smelling fluid was drained.

*Summary*—A Syrian woman, aged 52, had multiple recurrent hydatid cysts of the liver. She died following an operation for a secondarily infected abdominal cyst. The location of the intrathoracic cyst is not clear from the description. It may have been pleural or pulmonary.

CAMPBELL'S CASE<sup>83</sup> (1925)—A Russian woman, age not given, gave a history of gradually increasing thoracic distress. Examination showed well marked dullness over the lower left side of the chest with increased temperature, sweating and rapid pulse. The heart was displaced to the right. Exploratory aspiration recovered white, glairy pus. Rib resection recovered thousands of cysts varying from minute to very large. In the postoperative treatment, the patient was able to taste antiseptics used in irrigating. The cavity was slow in obliterating, and extensive resection of several ribs was done in order to decrease its size. Following the use of injections of bismuth paste, the patient made a fairly rapid recovery. She was again seen in September, 1919, with symptoms referable to the upper right portion of the abdomen. The roentgenogram showed a high diaphragm on the right side. An operation revealed a cyst below the liver, which after having been walled off with packing for nine days was enucleated at a second stage. It proved to be an echinococcus cyst.

*Summary*—A Russian woman, age unknown, had a suppurating cyst in the left pleural cavity containing daughter cysts. A pleurobronchial communication existed. It is not possible to determine from a study of the record whether or not this cyst had a pulmonary origin.

MAGATH'S CASE<sup>84</sup> (1921)—A man, age not given, was born in the United States, but had traveled in the Philippine Islands in 1908. He lived in Nebraska.

*Summary*—No details of this case report are available, as far as I can determine. The brief summary as given appears in a table of the Mayo Clinic cases reported by Magath.

ORTENBERG'S CASE<sup>84</sup> (1929)—A girl, aged 12, was first seen during November, 1923. She complained of pain in the lower right part of the chest, and she had a dry cough. The temperature was 102 F., the pulse was rapid. There was a hectic flush of the cheeks. No cyanosis or respiratory distress existed. At the base of the right lung posteriorly there was a rounded area of dullness over which the breath sounds were absent and the tactile and vocal fremitus were diminished. Ten days after the onset of the illness, during a fit of coughing, the patient nearly choked in the act of bringing up a large quantity of fluid together with what, according to the father's description, looked like a "small white, crumpled handker-

83 Campbell, C. C. Echinococcus, *Journal-Lancet* 45 572, 1925.

84 Ortenberg, S. Case Report, *Canad. M. A. J.* 20 284, 1929.

chief" The entire expectoration was returned in a tumbler and consisted of 5 or 6 ounces of a cloudy, watery fluid holding a partially suspended, gelatinous sediment. Microscopic examination showed an abundance of pus, elastic fibers and alveolar cells, but no hooklets. There was no hemoptysis. A puncture of the pleura was unproductive. Less than two years before this time, two echinococcus cysts had been enucleated from the liver. The roentgenogram of the chest three days after spontaneous excision of the cyst showed the presence of a dense homogeneous shadow about the size and shape of an orange, in the outer portion of the base of the right lung. The margins of this shadow were convex and fairly definitely outlined. The patient made a rapid recovery following the former. Roentgen study five weeks later showed a small area of mottling in the middle portion of the lower third of the right side of the chest. A third roentgenogram taken on Dec 5 1928, five years later, showed a circular shadow of calcification in the base of the right lung in the ninth interspace.

*Summary*—A girl, aged 12, gave the history of having had two echinococcus cysts removed from the liver. The cyst in the lower part of the right lung was expectorated and apparently cured by drainage through the bronchial tree.

#### ABSTRACT OF DISCUSSION

DR HOWARD LUBNATHAL, New York. I have had one case of hydatid cysts of the lung in a person who was born in Greece and who left there when he was very young, which brings up the point that is mentioned in the literature that people who have hydatid cysts have had them from early childhood, and that such cysts have never been proved to have developed after adult life. This may or may not be so. I should like to know what some of the other members of the society think about it. In case there is a calcification of the wall of the cyst I think that it is a good thing to divide the operation into two parts, first, take out the contents of the cyst and later, in an aseptic field, get rid of as much of the calcified capsule as possible.

I have drawn out the wall of what must have been enormous hydatid cysts from behind the sternum of one patient, taking out one piece every day or two until all had been extracted. The patient recovered. He came to the hospital with only a small sinus and nothing to indicate what had been the cause, it was not until I began taking out what I thought to be plates of bone that the diagnosis was made. I enlarged the incision and removed larger flat fragments. The curved form of the plates was suggestive. This operation was performed long ago, and no roentgenographic study was possible.

DR WILLI MEYER, New York. We are indebted to Dr Phillips for bringing this interesting subject before us. Cases of hydatid cysts are comparatively rare in our country. They are frequently found abroad, for instance on the southern shore of the Baltic Sea, a great many cases have been reported from there.

I remember a case in 1882, when I was a young doctor at the Surgical Clinic of Bowen University, in which the pleural cavity was punctured because all the symptoms pointed to an empyema. A yellowish, rather turbid fluid was obtained. The patient was operated on. Much to our surprise, a great many larger and smaller cysts floated in the fluid. It was a hydatid cyst of the pleural cavity. The patient recovered.

In the middle of the nineties, I did a catheterization of the ureters in a man.

The report on the obtained specimens came back from the pathologic laboratory with the emphasis that echinococcus hooks were found. In this case we had to deal with a hydatid cyst of one kidney. Unfortunately, the patient was not

operated on, but the specimen was absolutely convincing. Hydatid cysts can be found in any organ. The cases of Dr. Phillips show what one has to think of in making a diagnosis. In the presence of cysts, one should never forget the hydatid.

DR F. S. JOHNS, Richmond, Va. I had a case of this kind in a Virginian, a senior medical student who had been abroad two years during the World War. He came back with considerable loss of weight. One of our internists, Dr. Douglas Vanderhoof, found that he had a tumor of the right lung revealed by roentgen examination. I operated on him and found a calcified cyst, about the size of an orange. After the cyst was removed I sent the specimen around to several pathologists, which resulted in an undetermined diagnosis. About one year following the operation, fortunately or unfortunately an infection developed in the patient's pleura. The diagnosis was confirmed through finding the hooklets. After excision of the involved pleura he made a complete recovery. I reported this case several years ago before the Interurban Surgical Society, but it was not published. I should be glad to have Dr. Phillips add this case to his series.

DR POL N. CORYLLOS, New York. Dr. Phillips presented a remarkable study of the hydatids of the lungs. As I come from a country—Greece—in which hydatid cysts are a common occurrence, I wish to add only a word to that question. This is a word of warning against diagnostic tapping of these cysts. The patient is often highly sensitized by hydatid fluid, so that even a fraction of a drop entering the circulatory stream or even the subcutaneous tissue can produce severe anaphylactic shock. I will always remember a case of a young girl of 25, who nearly died after such an exploratory puncture. A second danger of these punctures, especially in the cysts of the liver, is the possibility of spreading about scolices and thus causing secondary echinococcosis, particularly in the peritoneal cavity. The same thing may occur in the pleural cavity, therefore I believe that Devé's method should always be used in these cases.

DR EDGAR W. PHILLIPS, New York. I think that every one agrees with what Dr. Lilienthal said about the age of infection, that is, that it occurs during childhood. Devé and Stonewell both emphasized that point.

Dr. Lilienthal spoke of the calcified pericystic layer, that is, the layer thrown out by the host surrounding the invader. When that is thick walled, the majority of surgeons drain the cyst cavity. In the lung, this pericystic layer is usually thin, and the lung cavity surrounding the hydatid cyst very rapidly obliterates so that they have been drained for a very short time in countries in which the disease is common.

Dr. Meyer emphasizes the rarity of hydatid cyst in this country. I do not know how long the cases are going to be rare if certain reports are true that in some instances 100 per cent of hogs slaughtered are found to have hydatid disease. We have reports from Virginia, where 100 per cent has been found, and scattered all over this country are reports of high percentages of infestation, particularly in hogs.

The chief of the Zoological Department, Bureau of Animal Industry, says that there is no way at present of knowing how much infestation there is in this country.

Dr. Coryllos spoke of the danger of anaphylaxis from aspiration. All of the reports I read on this subject condemned aspiration either for treatment or for diagnosis, both because of anaphylaxis and because of the danger of secondary sowing.

# GIANT SARCOMA OF THE PLEURA

## REPORT OF TWO CASES WITH REMARKS ON OPERATIVE EXPLORATION OF THE THORAX

HOWARD LILIENTHAL, MD

NEW YORK

CASE 1—*History*—Mrs I, aged 48, came to see me in December, 1929. Her family history was unimportant. About twenty years before, she had had the last of two miscarriages, which passed off without complication. She had borne no children. A number of years before, Dr H C Cowles of New York had extirpated a Bartholin's gland for gonorrheal infection, and in 1927 he removed the right adnexa, which were similarly diseased. The patient said that in 1927 there was a period when her legs became swollen without known cause. When I saw her, the swelling had completely disappeared.

In June, 1929, Dr Charles Gordon Heyd operated on her for cystic disease of the left ovary, removing a degenerated multilocular intraligamentous ovarian cyst. The operation had been difficult because of many adhesions to the hollow viscera, but the remainder of the abdomen had revealed no abnormality. Pathologic examination failed to show malignant disease. At that time Dr Heyd noted that the patient's fingers were greatly clubbed, and that the nails were incurvated. On examining her chest, signs resembling those of encapsulated fluid were discovered, and an exploratory puncture anteriorly resulted in the withdrawal of a little blood. The patient then stated that she had had pleurisy in her early youth and that it was a long time in healing. This statement is, of course, indefinite.

For a few years before I saw her she had had occasional spasmodic cough and had expectorated considerable quantities of tough mucus, sometimes flaked with blood. The attacks were asthmatic in character, but the wheezing was said to disappear on recumbency.

*Examination*—The patient was a tall woman in good general condition. The blood pressure was 135 systolic and 65 diastolic, but the vital capacity was only 22 liters, although her normal weight was 185 pounds (83.9 Kg).

Physical examination disclosed that in the lower half of the left part of the chest both front and back, there were the usual signs of encapsulated fluid. There was also great limitation in the extension of the right shoulder with the characteristic tenderness of subacromial bursitis. Although I did not believe that this had anything to do with the condition of her chest, I advised roentgen examination, which was carried out by Dr Leopold Jaches. He found the right shoulder to be normal. In the chest, however, there was a large area of localized density on the left side extending from the level of the second interspace in front almost to the diaphragm, but with a small clear space between the diaphragm and the opacity. Stereoscopically, this opaque region seemed to be limited to the anterior part of the chest, and Dr Jaches thought that the lower half of the upper pulmonary lobe was involved. There was pleural thickening and almost complete obliteration of the costophrenic sinus by what seemed to be a small quantity of fluid. The heart and other mediastinal organs were displaced

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1 The cases are not arranged chronologically.



Fig 1 (case 1) —Roentgenogram taken on Dec 6, 1929, before operation with the patient in an erect position The shadow resembles that of encapsulated fluid or tumor



Fig 2 (case 1) —Roentgenogram taken on the same date as figure 1 with the patient in the supine position The print was made with Bucky's diaphragm Note the clear space between the intrathoracic shadow and the diaphragm

to the unaffected side, and the left border of the heart could not be seen. There was no visible abnormality in the upper left part of the chest and none on the right side (figs 1 and 2). The aorta was normal. The right side of the diaphragm was restricted in its excursions. Dr. Jaques held the opinion that the density was probably produced by a tumor mass, but the presence of encapsulated fluid could not be excluded.

On auscultation, occasional squeaking dry rales were heard in both sides of the chest. It was evident to me that a full surgical exploration of the left side of the thorax should be made, but in order to gain as much information as possible I requested Dr. M. C. Myerson to examine the bronchial tree by endoscopy. He did this on Dec. 12, 1929, and, except for a slight bulging of the posterior wall of the bronchus of the left upper lobe into the lumen, nothing

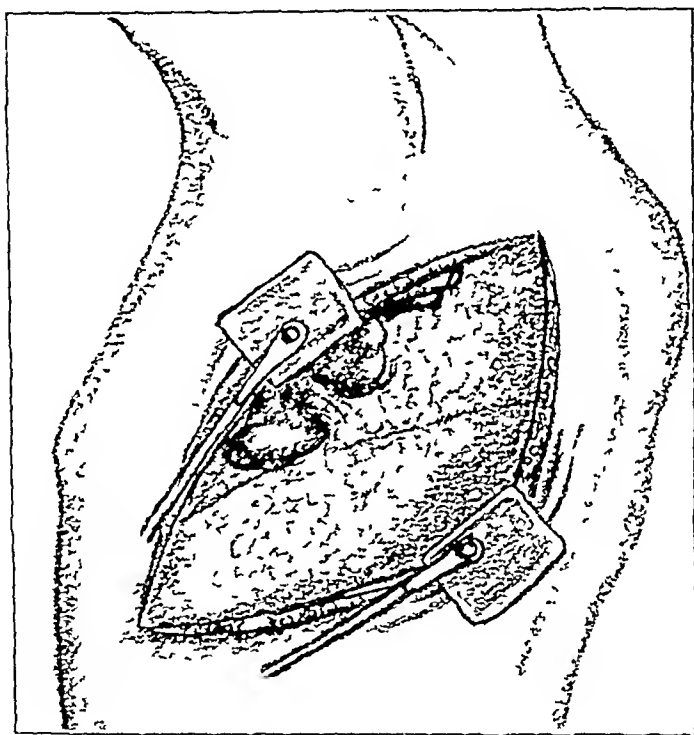


Fig. 3—Position of the tumor in case 1. The lung is shown running on to the surface of the growth. This sketch shows the posterior part of the tumor only. The ends of two ribs which were divided posteriorly are seen above. For simplicity's sake, only one rib spreader is shown in this picture, two were actually used.

abnormal was found. Dr. Myerson said that this deformity might have been congenital.

Considering this examination, I felt encouraged to operate in the hope that I might be able to extirpate a tumor or drain a chronic encapsulated empyema.

*Operation*—On December 24, the operation was performed. The anesthetic chosen by Dr. William Branower was a mixture of nitrous oxide and ethylene—no ether. Dr. Ira Cohen assisted, and Prof. Richard H. Meade of the University of Virginia, was present as an observer. The patient was placed on her right side, and the table was broken so as to widen the interspaces.

An incision of 7 inches (177 cm) was made between the eighth and ninth ribs, and immediately there was a gush of clear fluid from the pleura, so that at first I suspected that there was merely a sacculated pleural effusion. The rib spreader was put in, however, and at once a large tumor was revealed, pinkish gray in color and lying toward the mesial side of the lower portion of the upper pulmonary lobe (fig 3). The tumor appeared to have its origin in the edge of the lung. During my exploration, bleeding began from points that I could not see and, although this was not immediately alarming, it was disturbing in view of the contemplated radical procedure. It forced me to enlarge the incision and also to remove about 8 inches (20.3 cm) of the ninth rib for better exposure. The eighth, seventh and sixth ribs were divided posteriorly, the inci-

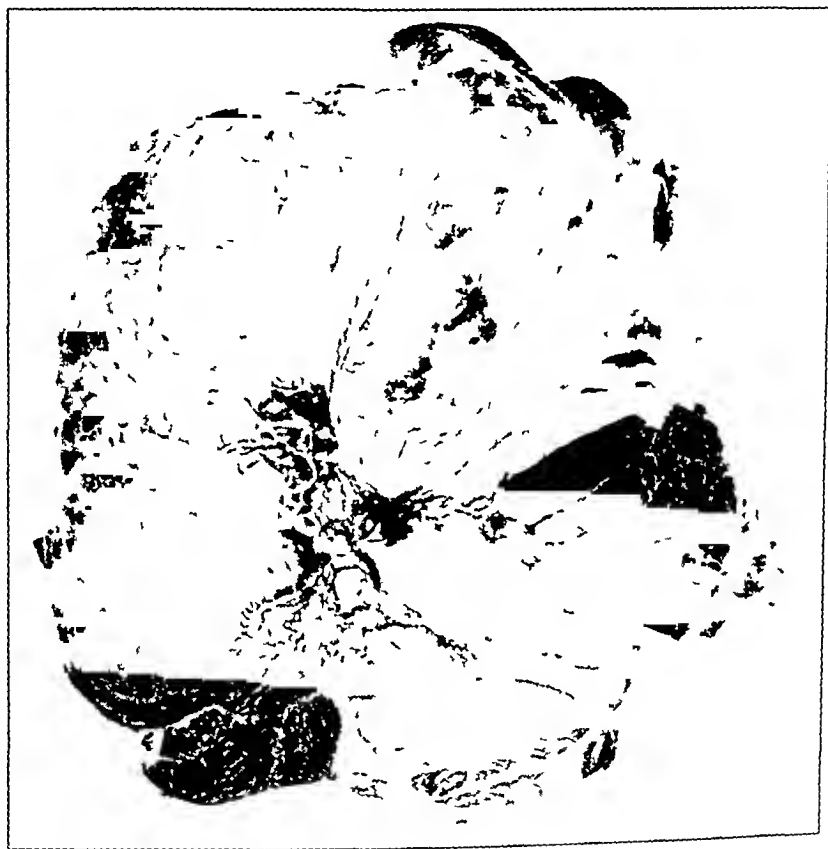


Fig 4—The specimen in case 1 after hardening. At the right is part of the lung which was resected. The mass near the center represents the stump of adhesions to anterior thoracic wall.

sion having been extended upward. Finally, two rib spreaders in different parts of the wound gave ample space for full intrathoracic manipulation. Minor adhesions were peeled away, and the tumor together with a small piece of the pulmonary edge was removed, the lung being divided distal to catgut ligature (fig 4). A large fleshy adhesion to the pericardium was ligated and cut through after the lung had been resected. The principal trouble was with the anterior adhesion that sprang from a point near the internal mammary artery, and which bled persistently so that the source had to be exposed by cutting the seventh rib near its cartilage. At Dr Ira Cohen's suggestion, a bit of free muscle was

placed against this bleeding area, and the oozing promptly ceased. All parts of the chest were now carefully explored by vision, but the only remarkable thing to be noted was the persistent collapse of the upper lobe which refused to expand even on intrapleural pneumatic pressure. I regarded this as probably the result of the long continued compression by the tumor.

A solution of dextrose, 1,800 cc, was injected into the vein of the right arm, and this was followed later by transfusion of 600 cc of citrated blood by Dr. Nathan Rosenthal, more as a prophylactic measure than as one of emergency.

The wound was closed with pericostal sutures of chromicized catgut, and the soft parts were sutured with silk, airtight. A small intercostal incision was made in the ninth space through which a fenestrated valve drainage tube emerged.

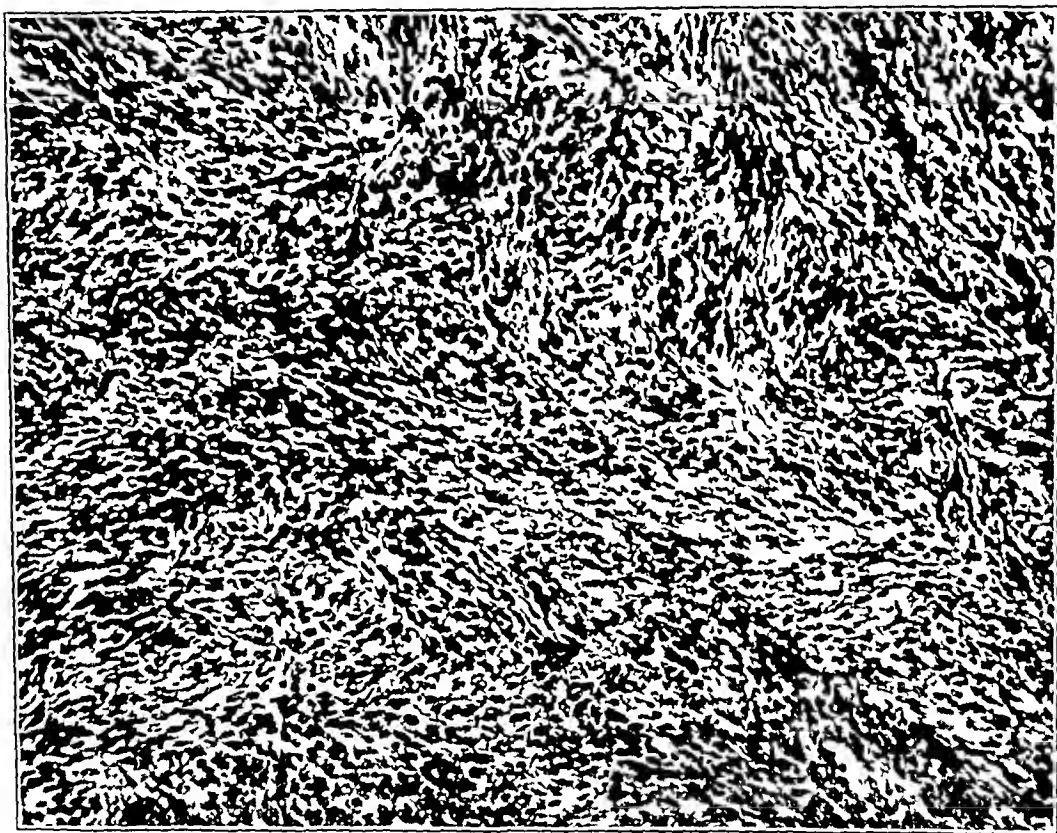


Fig. 5—Histologic slide from the specimen in case 1

*Course*—During convalescence, which at first was far from smooth, it was rather alarming to hear the sonorous râles in both sides of the chest which made one fear that a double bronchitis was present. The pulse, however, remained of excellent quality, and the patient's good general condition was maintained. Six days after the operation there was distress in breathing with some increase in the rapidity of the pulse, and fluoroscopy revealed a sacculated hydro-pneumothorax in the upper part of the chest. With the patient under nitrous oxide and oxygen, I reopened the lower half of the main wound and pushing away adhesions I opened a completely closed cavity containing air under pressure and about 1,000 cc of clear fluid.



In explaining this tense pneumothorax, I concluded that I was not dealing with a valvular condition, but that the tension was produced by the formation of a large quantity of fluid in the upper part of the chest where air had become encapsulated in the space left by the collapsed upper lobe. With the increase in fluid, the air was placed under tension. A small pulmonary fistula developed about ten days after the operation, and a low grade empyema resulted. The pleuropulmonary fistula closed spontaneously.

It is not necessary to go into further details of the convalescence. It was slow, and at the time this paper was written there was still a pinhole over which a tiny piece of gauze with one bit of adhesive plaster was worn as a dressing. The roentgenogram, however, indicated a sacculated pneumothorax and pleural thickening (fig 6). I fancy that nature will eventually bring about complete



Fig 6 (case 1)—Four months after operation. At this time the wound was a tiny fistula from which about two drops of fluid exuded in twenty-four hours yet there was considerable lateral pneumothorax and thickened pleura. The patient was practically well. There seemed to be an upward dislocation of the third rib, probably due to the transmitted force of the rib spreader.

obliteration of this air-filled space, though it is possible that an aseptic air pocket may remain for years, with no evil effect.

As a somewhat distressing complication, a number of teeth had to be extracted because of infection of the apical roots. Both shoulders were painful, and the subacromial bursitis had not entirely disappeared four months after operation, although the patient was in good general health and was gaining in weight.

NOTE—Now, more than seven months after the operation, the wound is soundly healed and the patient writes that she is in excellent health.

CASE 2—*History*—MAN B, aged 55, had been complaining for about two and one-half years of pain in his chest with remissions and recrudescences. There had been neither cough nor other distinctly pulmonary symptoms, but he had shortness of breath on exertion. The physical signs had been those of solidification in the lower left part of the chest, where there was a distinct bulging of the thoracic wall backward and outward. Fever had been absent, but there were general deterioration and progressive weakness. Roentgen examination revealed a semicircular shadow about 6 inches (15.2 cm) in diameter in the lower left part of the chest (fig 7). Dr. George Woolsey, who referred the patient to me, had operated about ten days before I saw him, resecting the ninth, tenth and eleventh ribs over the tumor. The mass proved to be extremely solid, and one rib was greatly broadened but not neoplastic. A cleavage plane permitted a specimen the size of a golf ball to be removed, and this was pronounced neurofibroma after examination in the laboratory of Roosevelt Hospital. Examination



Fig 7 (case 2)—Roentgenogram taken before operation showing the enormous fibrosarcoma of the lower left side of the chest

by an outside pathologist resulted in a diagnosis of fibroma or possibly fibrosarcoma of a low grade malignancy (fig 8).

At my suggestion, the patient was treated by injections of erysipelas and prodigiosus toxins (Coley's) which he bore well so far as his general nutrition was concerned, but the reactions depressed him so that after a few weeks this mode of therapy was omitted.<sup>2</sup>

There was general improvement, but about five months later I perceived a slight fetid odor at the patient's mouth and, fearing that there might be interference with bronchial drainage, I advised that the tumor be shelled out of its capsule if possible, and that the injections of the toxins be resumed.

<sup>2</sup> My reason for advising the toxic treatment was that I had had success in many cases of sarcoma with this form of therapy, and because Dr. Woolsey's description of his operation was not one which would make the surgeon anxious to attempt extirpation.

*Operations and Course*—The patient entered the Private Pavilion of Mount Sinai Hospital, and on Nov 23, 1926, I operated, using nitrous oxide and oxygen as an anesthetic. The operation proved beset with difficulties and could not be carried out as projected.

An incision about 6 inches (15.2 cm) long was made through the old scar. Bleeding was considerable, and it was difficult to resect the ribs on account of the trouble in securing the anomalous vessels in the tissues surrounding the tumor. Two ribs were finally resected, and the dense mass beneath was reached. I succeeded in removing a mass only about the size of a lawn tennis ball, and was then forced to desist because of large vessels which might have been injured within the depths. The case was obviously not radically operable. The

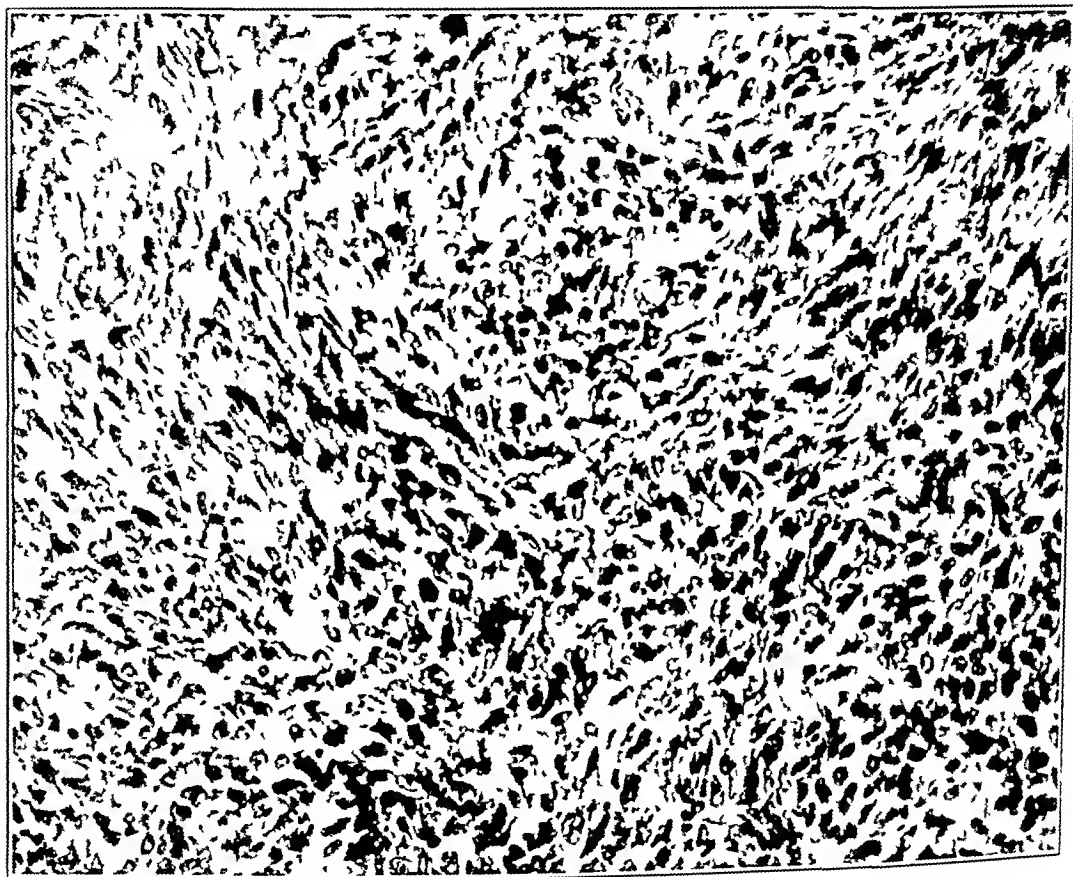


Fig 8—Photomicrograph of tumor in case 2, removed at the second operation

hollow was firmly packed with gauze, and the skin was closed over it by temporary sutures. These were removed three days later, and when the packing was removed smart hemorrhage appeared in the depths so that gauze had to be immediately replaced, this time soaked with thromboplastin. The patient's pulse rate, which was 80 before the operation, dropped to 76 twenty-four hours later. Pain was absent. I had hoped to remove more of the tumor with the aid of the diathermy monopolar knife but the electric appliance cut altogether too slowly for this kind of operation.<sup>3</sup> Roentgen therapy was then administered by Dr William Harris through the wound and later on, another course of erysipelas and prodigious toxins (Coley's) was begun, but had to be abandoned because of the patient's complaints.

<sup>3</sup> A more active cutting electric blade is now available

The wound healed from the bottom, and Mr B stated that his respiratory distress had been materially improved. He soon was up and about once more attending to his business.

Almost three years later, in February, 1929, the patient's weight was 120 pounds (54.4 Kg). His vital capacity was 2.8 liters. His blood pressure was 145 systolic and 85 diastolic. Roentgenograms revealed a shadow about as it was before my operation.

On April 1, 1930, the patient came to me again. He now weighed 8½ pounds (68 Kg) more than the previous year, but his vital capacity had dropped 0.6 of a liter (to 2.2) while the blood pressure had risen to 165 systolic and 90 diastolic. It is, however, recognized that in the case of this man, a sensitive person, the blood pressure readings at the office were probably higher than those of the patient's normal tension because of nervous apprehension.

I now found a rather puffy area over the posterior part of the tumor. There was slight cough but no expectoration. The general appearance was distinctly better than it had been. He again entered the hospital, and on April 24, 1930, I incised the old scar with a diathermy knife, easily shelling out the external softer part of the tumor which was of an entirely different consistency from that of the original new growth. With considerable physical effort, I then managed to enucleate a portion of the old tumor which was now extremely hard, and even seemed to be in some regions calcareous. The entire mass removed was about the size of a man's fist.

*Pathologic Report*—Dr Klemperer's report on the specimen is as follows: soft portions, "Polymorphous cell sarcoma with necrosis", firm portions, "hard fibroma".

"The soft portions of the tumor consist of very cellular areas in which the nuclei vary extensively regarding their size and chromatin contents. The paler nuclei resemble nuclei of fibroblasts, there are quite frequently cells encountered with very large intensely stained nuclei, often with two nuclei. The cellular areas blend with less cellular areas with abundant intercellular ground substance, but also here the irregularity of the cellular elements is very conspicuous. There are wide areas of necrosis and in the neighborhood of these, the tumor elements show a peculiar transformation whereby they become enormously enlarged with a bluish halo surrounding the markedly shrunken cells, the structure resembling cartilage. It is very possible that this is only a degenerative phenomenon. The intercellular substance is fibrillar and stains pink.

"The firm portions of the tumor are composed of a very dense tissue, very poor in cellular elements which resembles in its appearance the structure of a tendon. Here and there, however, one finds more cellular areas which also show a good deal of irregularities. The present tumor shows considerable differences from that removed several years ago which was a neoplasm of a uniform appearance."

The tumor, therefore, had undergone a great change for the worse. On roentgen examination, a circular shadow, probably that of a metastasis, was found in the contralateral lung (fig 9).

#### INCIDENCE

Giant sarcoma of the pleura or, more accurately, of the subpleural tissues, is extremely rare. The diagnosis is usually made on postmortem examination.

Klemperer and Rabin,<sup>4</sup> who collected a great mass of evidence from the literature, and who added cases personally observed by them, spoke of the solitary or localized form of subpleural connective tissue tumors. There seem to be two types, one, that of small tumors arising from the edges of the lungs, usually innocent small masses found at autopsy and not contributing to the fatal issue. There are also found in this region chondroma, fibroma and lipoma. The other is of a type which grows to gigantic proportions, even filling the chest, and causing death by mere bulk through circulatory disturbance. One case cited was that of a tumor 7 pounds (3.2 Kg.) in weight. These tumors usually originate beneath the costal pleura, my own case here reported (case 1), being



Fig. 9 (case 2)—Roentgenogram taken four years later, and immediately following third operation. The iodized oil gauze packing is faintly seen. There is now a secondary tumor in the opposite lung.

one of the rare exceptions and beginning on the visceral side, as in the case of the small tumors of accidental discovery. This type rarely, if ever, produces metastases in spite of the sarcomatous histologic appearances. Only twelve of these cases have been unearthed by Klemperer and Rabin, and a tabular study of these may be found in their paper.

My first case was typical in that the tumor was covered by what seemed to be an extension of the visceral pleura. It was nodular (fig. 4). Microscopically, the appearances were those of fibrosarcoma.

<sup>4</sup> Klemperer, Paul, and Rabin, Coleman B. Neoplasms of the Pleura. Mesothelioma and Fibrosarcoma, read at the 1930 meeting of the American Association of Pathologists and Bacteriologists. Dr. Rabin furnished me with data from his notes.

of fibroma with comparatively few tumor cells. Adhesions to surrounding structures were present, and in my second case, the exact origin of which could not be proved, the diaphragm as well as the pericardium was firmly adherent. This is the one which later changed its character, both clinically and histologically, and which produced a metastasis (fig 9).

#### COMMENT

At the 1923 meeting of this association, when I was president, the subject of my address was "Malignant Tumor of the Lung, and Necessity for Early Operation"<sup>5</sup>. In this paper I earnestly stressed the need for prompt intervention according to the surgical principles generally accepted in dealing with tumors elsewhere in the body. This was seven years ago, and the fellows of the association have shown diligence and interest in the study and surgical management of thoracic tumors. The association itself made a step forward by organizing a registry of neoplasms of the chest from which we shall certainly learn much. Yet the medical profession at large is slow to follow our lead, and it persists in the futile course of treatment by diagnosis, even to the final melancholy chapter of the postmortem report.

I have presented here two cases which speak for themselves. That the condition in both was histologically malignant merely emphasizes the validity of arguments for early and radical action. I will state here briefly a few apparently self-evident propositions associated with this subject, and will give my conclusions.

- 1 All tumors should be diagnosed
- 2 Tumors may be classified as malignant or innocent<sup>6</sup>
- 3 Tumors that are malignant should be extirpated
- 4 Tumors that are not malignant but that interfere with normal life, or with the happiness or welfare of the host, should be eliminated
- 5 An operation or other procedure that is more dangerous than the condition which it would relieve is unjustifiable
- 6 Intercostal diagnostic exploration through the normal thoracic wall, when performed under the principles of thoracic surgery, is not an extrahazardous operation<sup>7</sup>
- 7 Exploratory laparotomy is performed frequently with the consent of the internist or even at his suggestion

If the foregoing propositions are accepted, diagnostic operative procedures on the thorax should be the rule in the case of a tumor within the cavity of the chest, unless it is possible to learn its nature by other methods such as endoscopy or the biopsy of a metastasis.

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5 Lilienthal, H. Malignant Tumor of the Lung. Necessity for Early Operation, *Arch Surg* 8 308 (Jan) 1924.

6 The word nonmalignant may be used, but the designation of any abnormal growth as benign is erroneous.

7 It entails less shock and a far shorter period in bed than a laparotomy of equivalent magnitude.

8 A symptomless mass accidentally discovered by routine roentgenology does not, of course, demand immediate intervention even for accuracy of diagnosis but repeated observations should be made, and any increase in size or any onset of symptoms should be the signal for full investigation including, if necessary, exploratory operation. One may come on an essentially innocent growth, at the time removable, which, if left to itself, would increase in size and become hopeless.

A most instructive instance was presented at the pathologic conference of Mount Sinai Hospital on April 23, 1930, which profoundly impressed me. A man of middle age had entered the hospital eleven years before with signs of some endothoracic disturbance which led to roentgen examination. This revealed a clinically benign type of tumor

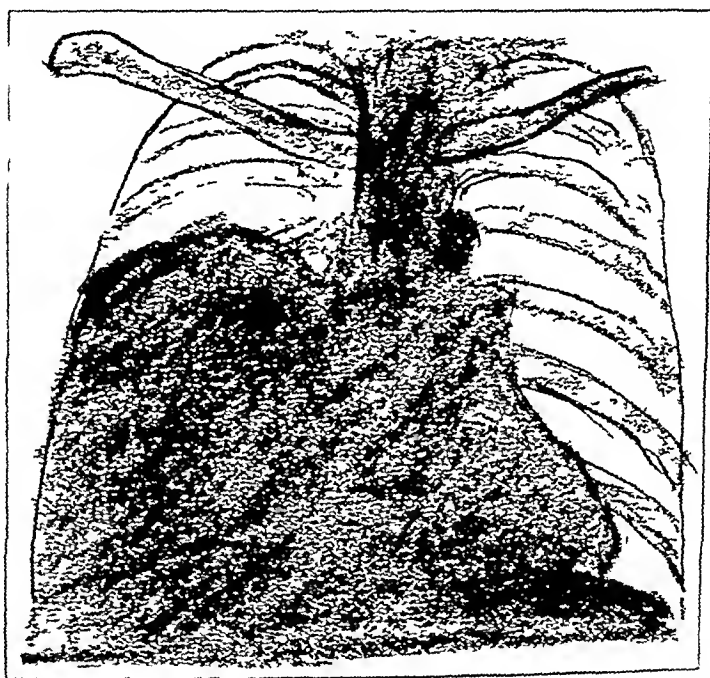


Fig 10—Huge lipoma of the lung, mistaken for cancer (clinically not roentgenologically). This is a rough sketch merely to give an idea of the size of the tumor at that time. (Tracing from Wessler and Jaches' *Clinical Roentgenology of Diseases of the Chest*, The Southworth Company, 1923.)

of the lung, probably involving the pleura. The patient had been in good health for over one year (fig 10).<sup>8</sup> A little bloody fluid was withdrawn from the chest by aspiration and the conclusion reached was that the patient was suffering from cancer of the lung.

This decision was strengthened by the presence of one or two vague shadows which were thought to indicate metastasis. After a number of years the man presented himself only a short time before his death with an enormous tumor producing embarrassment of the right side of

<sup>8</sup> Wessler, H. and Jaches, Leopold. *Clinical Roentgenology of Diseases of the Chest*. Troy, N. Y. The Southworth Company, 1923. p. 299.

the heart, from which he succumbed. The case was presented by Dr George Baehr. The specimen demonstrated by Dr Paul Klemperer was that of a gigantic lipoma arising in the subpleural tissue (fig 11). The state of the patient at his last admission forbade even minor diagnostic surgical measures but surely eleven, or ten or perhaps from five to three years before his last admission this tumor could have been removed or resected with little risk. Indeed nothing would have been

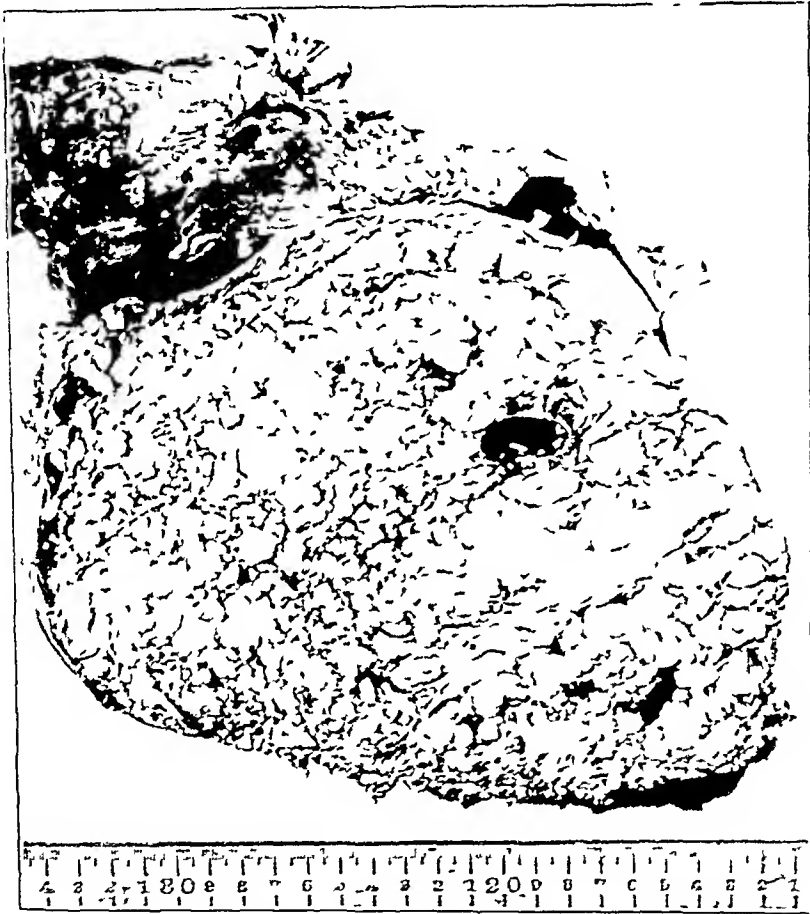


Fig 11 (case 2) —Postmortem specimen eleven years later (With permission of the Pathologic Department, Mount Sinai Hospital)

lost had an operation been undertaken for the sake of certainty at the time of his first examination. The fact that the man lived for so long a time with gradually increasing distress was not a reason for inaction.

Were this address intended solely for the fellows of this association, my presentation of the subject for a second time would be inexcusable. But my words will be read by others, and the paper may, perhaps, be abstracted by journals, so I trust that its message may be carried far beyond these walls.



## ABSTRACT OF DISCUSSION

DR C G HEYD, New York. The case that Dr Lilienthal has presented is of great interest by reason of the fact that the patient has been examined by at least six physicians. She was referred to me for a pelvic condition, and on doing a routine examination, I was impressed with the tremendous clubbing of the fingers. They were almost like the drumstick of a chicken. How it could be possible for the five physicians who examined her before I did not to note these fingers is rather surprising. Before she was operated on for the pelvic condition, roentgenograms of the chest were taken which showed the tumor exactly as Dr Lilienthal has indicated in his pictures. We were then in a difficult position. She had come to me for a pelvic condition. I did not disclose the tumor of the chest until after she had had a bilateral ovarian cyst removed. She made an uneventful convalescence from the laparotomy, and then we apprised her of the condition of the chest. Roentgenograms were taken in numerous positions, and the roentgenologist could not state what he thought the tumor was. I should like to ask Dr Lilienthal if a preoperative roentgen diagnosis as to the character of the tumor was made.

DR HOWARD LILIENTHAL, New York. No.

DR C G HEYD. That was our difficulty. At about the same time one of our nurses came to me because of a goiter, she exhibited almost the same clubbing of the fingers, only not to such an extent, and she had a shadow almost identical with that which the patient presented. We told her that the condition of the lung was of far greater significance than the goiter. The result was that she had nothing done and is still going about her duty with a progressive enlargement of the fingers.

It is a distinct pleasure to have followed this case of Dr Lilienthal's, and it is surprising to note the apathy of the medical profession in regard to lung pathology as the physician sees patients with clubbed fingers from time to time, which are an open invitation for an investigation of the chest. I congratulate Dr Lilienthal on his excellent result.

# INTRATHORACIC TUMORS

## REPORT OF CASES

I. C. DAVISON, M.D.

ATLANTA, GA.

It is not my intention to present in detail a textbook discussion of tumors of the chest, but after a brief general discussion of the subject to report a series of cases that have occurred in my private practice and that have been observed at the Stenck Clinic of Atlanta. Intrathoracic tumors are more common than formerly reported and are divided into primary and secondary.

Primary tumors may be benign or malignant. The benign group, including lipoma, chondroma, osteoma, fibroma, fibropapilloma and dermoids is rare. Benign tumors may occur in the mediastinum or in the lungs. The diagnosis of nonmalignancy cannot be made at once but only after prolonged observation when if the tumor has not increased in size and if it retains its regular sharp outline with no increase of symptoms, a diagnosis of nonmalignancy may be made. Benign tumors may produce pressure symptoms that are distressing and at times pulmonary suppuration and sepsis by partial or complete obstruction of the bronchi. In the malignant group carcinoma is the most frequent. Statistics by various authors as to its incidence vary from 1 to 10 per cent of all cancers. Certainly a higher percentage is being diagnosed now than was formerly thought to exist. This may be the result of more thorough examination and the more frequent use of the x-rays and the bronchoscope. Primary carcinoma of the lung may be endobronchial or parenchymatous, the bronchial type being the more common. It occurs more frequently in males than in females, the ratio being given by Fishberg as 2:1, and other authors estimate an even higher ratio. Chronic irritation must be considered as the principal cause of primary cancer of the lung, this being produced in many cases by the inhalation of irritating substance, such as dust by miners and stone cutters and irritating gases and tobacco smoke. Chronic bronchitis, tuberculosis, asthma and influenza may be forerunners of cancer of the lung. It at times occurs in connection with pulmonary abscess and bronchiectasis, and it is impossible to say which is cause and which is effect. Cancers of the lung occur most often late in life or after 60 years of age, but they have been observed in young adults. Ewing reported 80 per cent as occurring in the upper lobes of the lungs. The pathologic process may invade the contiguous tissues and organs by infiltration and by partial or complete obstruction may result in bron-

chiectasis, atelectasis, gangrene, abscess, empyema and hemorrhage. The tumors may metastasize through the lymph or blood stream to any portion of the body. Tuffier believed that metastasis takes place early, this is not concurred in by others. The most frequent locations of metastases from primary cancer of the lung are the bronchial glands, liver, bones, brain and cervical and thyroid glands.

Practically all secondary tumors of the lung are malignant and are metastases deposited by the blood and lymph streams in the pulmonary parenchyma from some distant primary focus. They may be single or multiple and grow into spheroidal masses which may reach great size and retain their sharp outline for a long time. The course of secondary carcinoma of the lung is somewhat similar to that of primary, only it is usually more rapid, as the patient probably has already become anemic and depleted by the primary condition. The signs and symptoms of cancer of the lung are not very different from those of other pulmonary conditions but they tend to persist and progress in spite of treatment. The symptoms at first may be rather vague and indefinite, more of a sensation of gradually increasing ill health, with slight cough. Later there is pain in the chest which may be referred to the shoulder and down the arm on the affected side. The cough becomes increasingly productive and more severe. The sputum may be slightly streaked with blood, but has no fetid odor. The physical signs may be misleading even in advanced cases. Usually they resemble the signs of tuberculosis, unresolved pneumonia or fluid in the pleural cavity. There may be some elevation of temperature even before a mixed infection is present. Tubercle bacilli are sometimes found in the sputum, as the two conditions may coexist. The blood is not characteristic, there is usually a moderate leukocytosis, but anemia frequently develops late. Clubbing of the fingers and toes is present in many cases, particularly if there is bronchiectasis or abscess as a complication. The diagnosis, as a rule, cannot be made from the history and the physical examination alone, but these are very important. The bronchoscope is a valuable aid in diagnosing pulmonary tumors and should be used early in cases in which tumor is suspected. It is not a dangerous procedure, and should not be reserved for use as a last resort.

Many of these tumors have their origin in the mucosa of the bronchi and a fragment from a suspected area can easily be removed for biopsy through the bronchoscope, thus clearing up the diagnosis. This can often be done before the x-rays show anything definite. Roentgen examination has been our chief aid in diagnosing tumors in the thorax, it has often revealed the presence of tumors that were not suspected. In cases in which a tumor is thought to be present both anteroposterior and lateral views should be made. Fluoroscopic should be done in all

cases. Sarcomas are hard to differentiate from carcinomas and are only one-fourth as frequently observed.

In every case in which thoracic tumor is suspected a careful history should be taken and a thorough physical examination made with the idea of locating any obscure primary focus or metastatic nodules from which microscopic specimens may be obtained for diagnostic purposes.

Röntgen therapy has been used extensively in cases of suspected and proved malignant tumors of the mediastinum and lungs. It usually has a palliative effect causing temporary improvement. Occasionally a case is reported clinically diagnosed as malignant which has responded readily to röntgen irradiation. Schroeder of Cincinnati reported such a case with remarkable recovery and the röntgenograms appear in Dr. Lilienthal's book. At the Steiner Clinic in Atlanta röntgen therapy is used as a routine measure for its palliative effect only.

Surgical intervention offers the only hope for recovery from an early neoplasm of the lung. After removal of the tumor-bearing area healing should occur without infection. The so-called dead space is obliterated by the elevation of the diaphragm, the contraction of the thoracic wall and possibly by a physiologic emphysema of the remaining pulmonary tissue.

In selecting patients for operation, the bronchoscope and the x-rays should be the main guides. The location of the tumor in the lung will also influence the operator's decision, those in the periphery being more accessible than those located nearer the bronchial tree. The end-results depend on how early these cases come to operation, and unless the surgeon has the sympathetic cooperation of physicians, patients with malignant tumors of the lung will continue to reach the surgeon too late for cure. In extensive operative procedures on the lungs, Sauerbruch advises a two stage operation. At the first the necessary rib resection is done and the pulmonary artery controlling the affected lobe is ligated. At the second stage, three or four weeks later, the diseased area is extirpated.

In late cases, palliative operations may be performed on selected patients such as partial collapse of the affected lung, evacuation of secondary abscess of the lung and resection of a large portion of the tumor, which in certain cases may give temporary relief from distressing symptoms.

In operations on the lung, its vascularity is somewhat of a handicap. The high frequency radio-knife and coagulator can be used to advantage. Lilienthal advises exposure of the tumor, curetting or scooping out of the contents and packing with gauze. The gauze is left in place several days and then changed daily. Slough will be cast off, and later the area can be treated with the x-rays or radium.

## REPORT OF CASES

CASE 1—(Case reported to the Fulton County Medical Society by Dr R S Leadingham, pathologist to Grady Hospital) A white man, aged 20, was admitted to the Grady Hospital on Feb 7, 1930. The chief complaints were orthopnea, cough and edema of the lower extremities. As the patient was admitted to the hospital acutely ill, no history was attainable.

Examination revealed enlarged cervical glands. The patient was somewhat cyanotic and unable to lie down on account of difficult breathing. Mediastinal dulness extended from the right sternal margin to the left axilla. There were



Fig 1 (case 1)—Lymphosarcoma of the thymus gland

moist rales over the bases of both lungs. The heart sounds were muffled, and there was a soft systolic murmur at the point of maximum impulse. The pulse rate was 120 and regular, and the volume was fair. The systolic blood pressure was 122 and the diastolic 84. The temperature on admission was 98.4 F, and the respiratory rate, 24. The white blood cells count was 17,000, with 68 per cent polymorphonuclears. Roentgen examination showed a large tumor mass occupying a greater portion of the left side of the chest and mediastinum, displacing the heart to the right.

Twelve hours after admission the temperature was 102 F and the pulse rate, 120. The patient died suddenly four hours later.

At autopsy, a large mediastinal mass was found extending from above the clavicle to the superior surface of the heart and displacing both the heart and the great vessels. Microscopic sections showed lymphosarcoma of the thymus gland. The lymph nodes of the mediastinum and retroperitoneal regions were enlarged, and there were several soft nodular masses in the right lung. On the surface of both kidneys there were single small nodules 1 cm in diameter. No metastases were found in other tissues of the body. There were scattered areas of broncho pneumonia in both lungs.



Fig 2 (case 1)—Gross specimen of figure 1 showing heart and blood vessels displaced downward by the tumor

CASE 2—Mrs V S, aged 53, married, was admitted to the Steiner Clinic on Jan 17, 1930, with the complaint of pain in the back and the left side of the chest and a tumor on the left side. The present illness began about eighteen months before admission, when the patient noticed a pain in the side and back, it was intermittent at first and gradually grew worse. Ten months before she noticed a lump or a tumor on the left side, just posterior to the axilla. At the time of admission the pain was in the left side near the breast and was severe. The patient took six acetylsalicylic acid tablets daily for relief.

She had had the usual childhood diseases. She had had an operation for ovarian tumor (?) when 20 years of age. The menopause occurred when she was 47.

Her father died of nephritis and her mother died at 60 of "rheumatism," but had had an operation for tumor of the breast four years previously

The tumor presented by the patient was small (3 by 4 by 2 cm), it was located in the left posterior axillary fold, and was not attached to the ribs. It was not tender on examination. There were palpable glands in the left axilla and supraclavicular space, but none on the right side. A roentgenogram, taken on January 17, showed the tumor in the left axillary region with destruction of a portion of the sixth and seventh ribs, probably a cyst producing pressure necrosis.

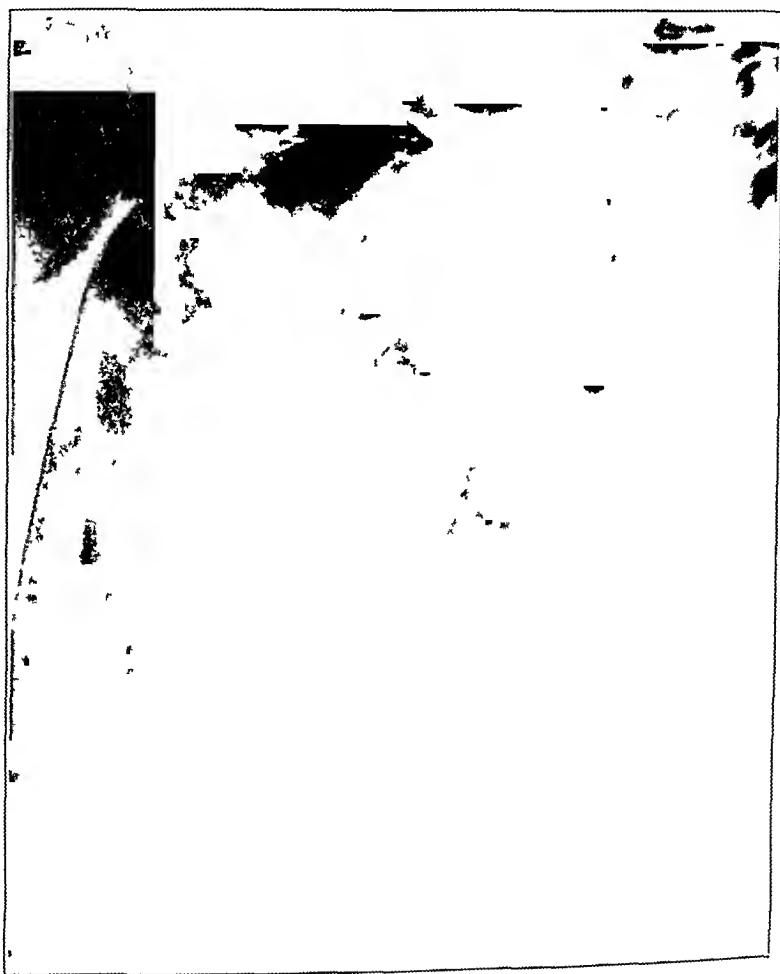


Fig 3 (case 2) —Myxo-angio-endothelioma showing destruction of the sixth and seventh ribs

There were 3,760,000 red blood cells, 70 per cent hemoglobin, 8,050 white blood cells and 65 per cent polymorphonuclears, 31 per cent being small. The results of urinalysis were essentially negative.

On March 24 1930, a section from the wall of the cyst showed myxo-angio-endothelioma, evidently arising from the pleura.

A diagnosis of myxo-angio-endothelioma was made. Roentgen irradiation, five treatments, was given in January and February, with no improvement.

A recent roentgenogram showed that the disease was progressing rapidly in spite of treatment. The patient is still under observation.

# DAISON—INFLAMMATORIC TUMORS

CASE 3—Mr T T, aged 60, complained of cough, raising of sputum, anorexia and loss of weight for a period of two months. There was no family history of cancer. He had never had pneumonia, bronchitis, asthma or any thoracic disease, and had been well until the present illness. He had had three severe head colds three months before the onset of the present symptoms, but did not go to bed. Loss of appetite began with a cough, and at this time he began to lose weight. He had no pain at any time. Four months after the onset, the cough and loss of weight had progressed greatly, and he raised a large quantity of foul sputum. He then came to the hospital, where he was kept continually in bed. The odor of the sputum became worse. The temperature reached 100 F daily. The measured amount of sputum was from 200 to 500 cc in twenty-four hours, respirations ranged from 22 to 26 and the pulse rate from 88 to 108, the urine was normal, and the leukocytes on admission to the hospital numbered 18,000. Two



Fig 4 (case 3)—Primary carcinoma of the lung, coexisting with abscess

months later they were 32,000, the red blood count was 2,800,000, and the Wassermann reaction was negative.

A diagnosis of abscess of the lung was made. Drainage was established, and 60 cc of very foul pus was obtained. The patient died three days later. Partial necropsy revealed primary carcinoma of the lung.

CASE 4—Mrs E F, aged 66, was admitted to the Grady Hospital on March 1, 1930, complaining of pains in the chest, hematemesis, pain in the head, cough with dyspnea and night sweats. The present illness began with pain in the epigastrium for several months. For the past three months, there had been pain in the head. On Feb 26, 1930, the patient vomited blood, and had been spitting up some blood since. On March 1, she coughed up about "one quart of bright red blood." She had had typhoid fever at the age of 12. Both breasts were removed thirty-three years previous to admission. The patient was told that the breasts were not malignant. She had had influenza in October, 1929, and the cough had persisted since that time. The family history was unimportant.



On March 22, the red blood count was 3,530,000, with 75 per cent hemoglobin, the white blood count was 10,500. On April 9, 125 cc of coffee-colored fluid was aspirated from the ninth interspace in the posterior axillary line. A twenty-four hour culture showed no growth. A roentgenogram on March 4 showed a large round mass in the upper left side of the chest with an opacity at the base of the left lung. The heart shadow was displaced to the right. The picture was suggestive of a new growth.

The diagnostic impression was sarcoma, cyst or syphilis.

A roentgenogram of the chest on March 26 showed increased density from the second interspace almost to the diaphragm on the left side. The density was homogeneous and was probably a new growth arising from the mediastinal region.

Examination revealed an anemic woman, apparently in constant pain. She coughed occasionally and spat bright red blood. The heart could not be per-

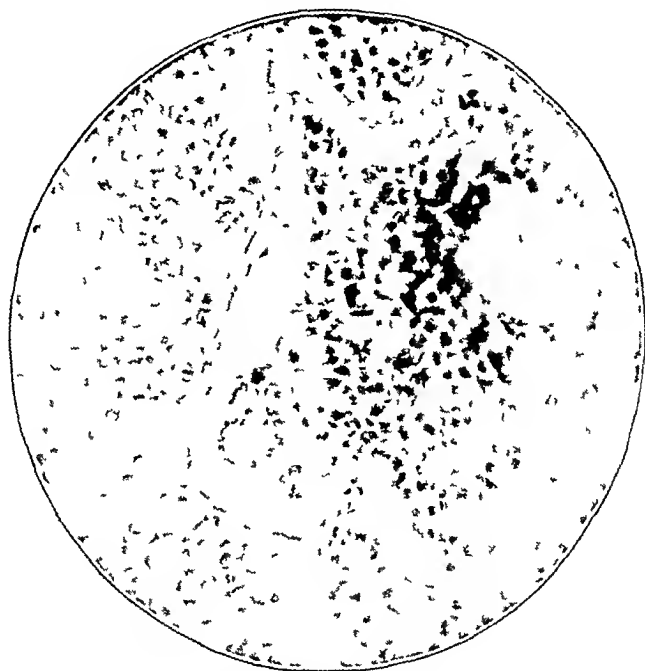


Fig 5 (case 3)—Carcinoma of the lungs. Same as figure 4.

cussed and outlined owing to pain. There was partial heart block with an occasional dropped beat. The vessels were sclerosed. The systolic blood pressure was 85 and the diastolic 65. A systolic murmur was noted. There was a definite area of dullness and diminished tactile fremitus extending from the midline to the left thoracic wall, which occupied the middle third of the chest. Expansion on this side was definitely limited. A few fine moist rales were heard over this area of dullness. The right lung was normal.

Diagnosis of primary mediastinal cyst was made.

This patient is in the medical service, and because the blood shows a 4 plus Wassermann reaction she is receiving antisyphilitic treatment and is rapidly growing worse. The pathologic process in the lung is becoming more extensive which, in my opinion, proves that the primary condition is not syphilitic.

CASE 5—Mr D. H. L., aged 53, married, was admitted to the Steiner Clinic on Oct 21, 1929, complaining of pain in the left side of the chest, yellow, foul

irony sputum, loss of weight and moderate anemia. The present illness began with pain in the left side, which had continued for the past fourteen years. Blood-streaked sputum had been expectorated at times, but not recently. The patient had lost weight in the past three years. He had been under treatment by various physicians and had taken antisyphilitic treatment over long period of time, with no apparent benefit. He had had pneumonia one year before admission. He had lost 50 pounds (22.7 Kg) in the last three years.

Examination revealed a distinct bulging in the upper portion of the chest with large varicose veins over the sternum and anterior portion of the upper part



Fig 6 (case 4)—Primary mediastinal cyst

of the abdomen. The breath sounds, voice sounds and tactile fremitus were increased over the right side of the chest. A few moist rales were heard. There was a mass the size of a small orange in the right lower quadrant of the abdomen. The red blood count was 3,580,000, with 76 per cent hemoglobin. The urine was normal. The Wassermann reaction was negative. The roentgenogram showed a shadow, apparently enlarged glands of the mediastinum or a primary cyst, possibly a dermoid.

A probable diagnosis was made of a dermoid cyst of the mediastinum pressing on the superior vena cava.

The patient is still under observation.

CASE 6—Mrs B L, aged 51, married, was admitted to the Steiner Clinic on Aug 12, 1929, complaining of polyuria and dysuria, edema, loss in weight and pain in the left side of the chest since May, 1929. The present illness began gradually twelve months before admission. The past history was unimportant, except for amputation of the breast five years before. The patient was told that it was not malignant.

Examination of the chest gave negative results. The extremities showed a clubbing of the fingers with enlargement of the joints, especially the phalangeal joints. The patient looked acromegalic. The systolic blood pressure was 132.

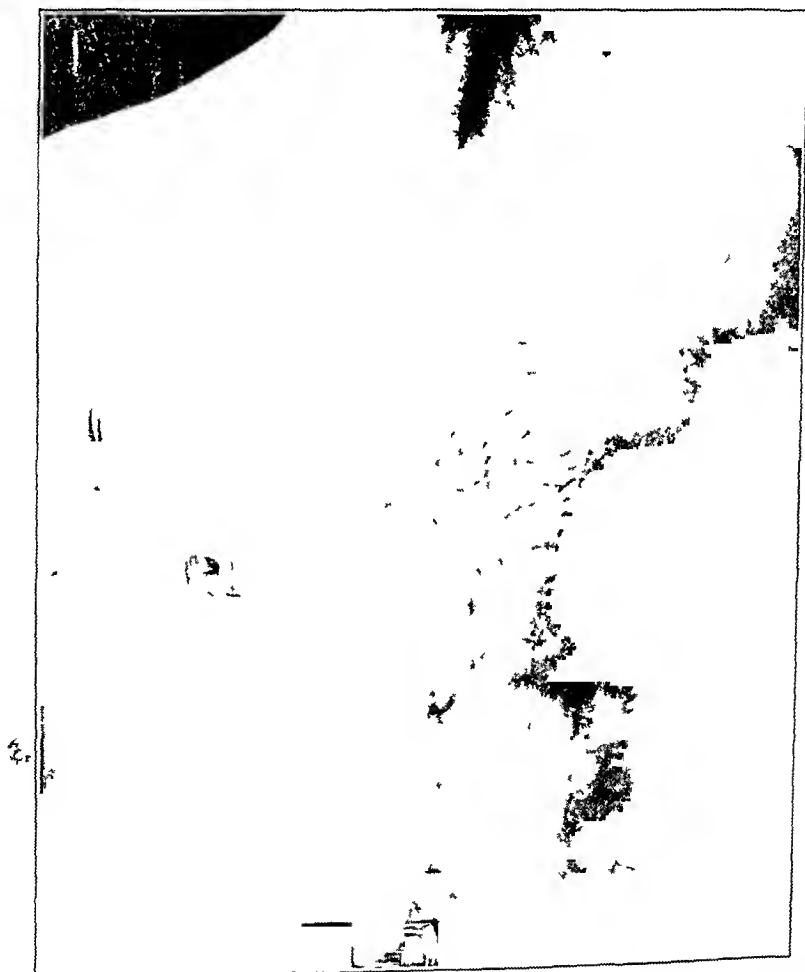


Fig 7 (case 5)—Mediastinal tumor obstructing the superior vena cava, varicose veins on the anterior surface of the chest and abdomen

and the diastolic 68. The red blood count was 2,480,000. The Wassermann reaction was negative. A roentgenogram showed a sharply defined homogeneous shadow of increased density the size of a grapefruit in the base of the left lung.

The diagnostic impression was that probably a benign cyst was present. A roentgenogram of the long bones showed chronic arthritis and chronic productive periostitis. The patient died in November, 1929. Permission for autopsy was denied.

The final diagnosis was uncertain, but the condition was probably a benign cyst of the left lung.



Fig 8 (case 5) —Same as figure 7, showing mediastinal tumor



Fig 9 (case 6) —Cyst of the lung, probably benign

CASE 7—A T, a schoolgirl, aged 11, was admitted to the Steiner Clinic on Dec 3, 1926, complaining of pain in the left upper part of the chest and general weakness. The present illness began with these symptoms, which had existed for several years and had gradually progressed. The patient was healthy until the age of 6. Her parents noticed that she was not growing as fast as her older sister, she became weak and would not play as other children. Recently, she complained of pain in the left upper part of the chest. She had had a fast pulse, and her color had not been good. A roentgenogram of the chest on March 24, 1924, showed a tumor of the mediastinum. She was given several doses of arsphenamine and also roentgen treatment before being admitted to the clinic.

Examination revealed a rather pale girl, aged 11, undernourished and undersized. There were several enlarged glands under the angle of the jaw on both



Fig 10 (case 7)—Cyst of mediastinum of several years' duration, probably benign

sides. The chest showed thin only fair, symmetrical expansion, owing to pain on deep inspiration. There was slight diminution of resonance over the left scapular region and decrease in breath sounds over the same area. No rales were heard. It was impossible to outline by percussion the tumor shown on the X-ray films. The red blood count was 4,000,000, with 78 per cent hemoglobin, the white blood count was 12,850, with 61 per cent polymorphonuclears. A roentgenogram of the chest on Dec 14, 1927, showed a large, sharply outlined spheroidal-shaped shadow or mass in the upper left side of the chest, continuous with the mediastinum. The mass on lateral exposure appeared in contact with the ribs behind.

A diagnosis of benign cyst of the mediastinum (primary) was made. The patient is still under observation.

CASE 8—Pat C, aged 3, was admitted to the Steiner Clinic on Dec 6, 1929, the chief complaint was hematuria and a mass in the right side of the abdomen. The present illness began on November 24, when the patient passed bloody urine, he continued to pass it daily since that time. On December 1, a mass was noticed in the right side of the abdomen which was not sensitive or painful.

Examination revealed a large firm mass in the right side of the abdomen, extending from the lower border of the ribs to the crest of the ilium. The abdomen was slightly distended. The right kidney could not be outlined separately from the mass. The left kidney was not palpable. The spleen and liver were apparently normal. The diagnostic impression was (1) sarcoma of the right kidney and (2) hypernephroma.



Fig 11 (case 8)—*A*, sarcoma of the kidney with early metastases to the lungs; *B*, same as figure 11 *A* following the Coffey-Humber treatment, showing extensive and advanced metastases to both lungs.

The patient was given several roentgen treatments, the mass was reduced somewhat in size, and the hematuria had ceased. The parents were advised as to the gravity of the case, and decided to take the child to San Francisco for the Coffey-Humber serum treatment (Feb 14, 1930). They remained in San Francisco three weeks, during which time he received six treatments. He had a violent reaction following the second injection, and was very ill for several days. The tumor grew rapidly, and the patient was much worse after the treatments, in fact, the parents were advised that he could live only a few days. Against the doctor's advice, he was brought home. Later he improved, and is again being treated by roentgen irradiation. On April 16, 1930, marked dyspnea developed, and a roentgenogram showed widespread involvement of both lungs. Eight treatments have

been given, with marked relief from the dyspnea and reduction in the size of the tumor. It is expected that the irradiation is only palliative.

A diagnosis of sarcoma of the right kidney with metastasis to both lungs was made.

CASE 9—Mrs. C. D., aged 38, married, was admitted to the Steiner Clinic on April 20, 1927, complaining of intermenstrual bleeding, profuse menstrual periods and weakness. The present illness began four months before admission, when the patient noticed a slight bloody discharge or "spots" between periods, and recently her periods had been more profuse than usual. She had been growing weaker gradually for several months.

Examination of the chest gave negative results at the time of admission. The cervix was enlarged, with bilateral lacerations, and was eroded. It bled

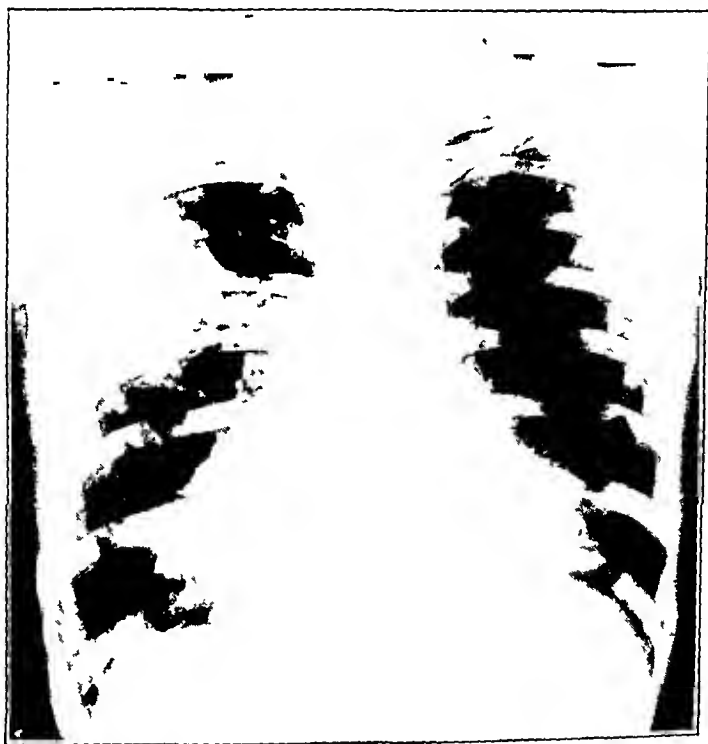


Fig. 12 (case 9)—Secondary carcinoma of the lungs metastasized from the cervix uteri.

easily (apparently malignant). Otherwise physical examination gave negative results. A section from the cervix showed epidermoid carcinoma of the squamous type. A roentgenogram of the chest on April 20, 1928, showed metastatic carcinoma of the upper and outer portion of the left lung and also in the base of the right lung. On April 22, 1927, the red blood count was 4,000,000, with 75 per cent hemoglobin. On April 25, 1928, the red blood count was 2,800,000, with 40 per cent hemoglobin.

A final diagnosis was made of carcinoma of the cervix with secondary metastases to the lungs.

Radium was applied to the cervix, and roentgen therapy to the pelvic region in April and May, 1927.

On April 20, 1928, the cervix had healed entirely. The patient has symptoms of pulmonary complications, and the roentgenogram showed metastatic carcinoma,

which was unusual, with a primary lesion situated in the cervix uteri. In May, 1928, roentgen irradiation of the chest was instituted. The patient died on May 20, 1928.

Autopsy showed metastatic epidermoid carcinoma and bronchial pneumonia.

CASE 10—Miss E. J., aged 27(?), was admitted to the Steiner Clinic on August 7, 1925, complaining of sore throat, swelling on the left side of the neck, difficulty in swallowing and pain in the left ear. The present symptoms began about two months before admission, and had been progressive.

Examination revealed a moderate swelling on the left side of the neck, due to an enlargement of the cervical glands. A roentgenogram on August 7 showed in the third interspace on the right side an area of increased density, which was homogeneous, had smooth edges and extended from the mediastinal space half way to the periphery of the lungs.

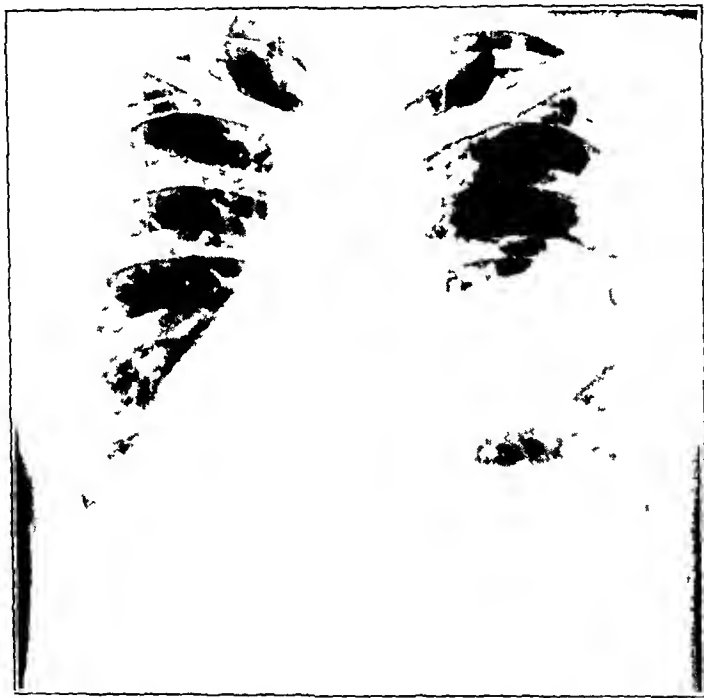


Fig. 13 (case 10)—Endothelioma of the lymph nodes with metastases to the lung.

The diagnostic impression was probably lymphosarcoma(?).

On August 8, biopsy of a lymph node, removed from the neck under procaine hydrochloride, showed endothelioma of the lymph nodes.

A final diagnosis was made of endothelioma of the lymph nodes with secondary metastases to the lungs.

Roentgen irradiation was employed on August 12, October 9, 12, 22 and 26. A roentgenogram on October 5 showed that the area had materially increased in size and that there was a new area just outside the heart shadow in the base of the left lung.

According to follow-up notes made on Nov. 4, 1925, the patient had been noncooperative from the beginning, had visited all the quacks and had not kept her appointments. She had a slight hemoptysis for two nights, decided that she had pulmonary tuberculosis and left for Los Angeles. The results are unknown.



CASE 11—R L, a Negro, aged 70, was admitted to the Steiner Clinic in August, 1925, complaining of a mass in the left side of the neck, enlarged glands of both the axillae and groins and dyspnea and cough. The present illness began in April, 1925, when the patient noticed a small lump on the left side of the neck which was not painful. Later other lumps appeared in the groins and axillae. The original growth progressed.

Examination showed a huge mass of enlarged glands on the left side under the ear, 10 by 8 by 6 cm. The tumor was firm and smooth, it was not attached to the skin, and was not tender. There were several smaller nodes on both sides of the neck which were freely movable. There was marked dulness in the apex of the right lung, sounds were normal, and no râles were present. There were enlarged glands in both axillae, not attached to the skin, and freely movable. Several enlarged, freely movable glands were found in each groin. A roentgeno-



Fig 14 (case 11)—Hodgkin's disease

gram of the chest on August 19 showed the right apex to be filled with dense shadows.

The diagnostic impression was (1) Hodgkin's disease and (2) lymphosarcoma. In August, 1925, a small node was removed from the groin for diagnosis. A diagnosis of Hodgkin's disease was made.

Roentgen irradiation was given, with some improvement. The patient died in the summer of 1926 with acute diarrhea.

CASE 12—Henry A F S, white, was admitted to the Steiner Clinic on Feb 18, 1928, complaining of loss in weight, lumps under the arm and in the neck, weakness and loss of appetite. The present illness began when the patient "caught cold" in September, 1927. He later noticed the appearance of the masses in the arm pits and neck, and gradual loss in weight, weakness and lack of appetite.

Examination revealed that the glands of the neck were markedly enlarged and matted together, but were not sensitive to palpation. The glands of both axillae were enlarged. There was increased dulness on either side of the mediastinum,



Fig 15 (case 11)—Same as figure 14, showing involvement of the mediastinal glands



Fig 16 (case 12)—Hodgkin's sarcoma with metastases to the lungs

with a few scattering râles. Roentgenograms showed widespread involvement on either side of the sternum, extending well out to the periphery of both lungs at the bases.

The diagnostic impression was (1) lymphosarcoma and (2) Hodgkin's sarcoma. A gland was removed from the neck and a microscopic examination made. A diagnosis of Hodgkin's sarcoma with metastases to the lungs was made.

Roentgen treatment was given, with material reduction in the size of the masses. The patient died on April 22, 1928. Autopsy showed widespread Hodgkin's sarcoma throughout both lungs.

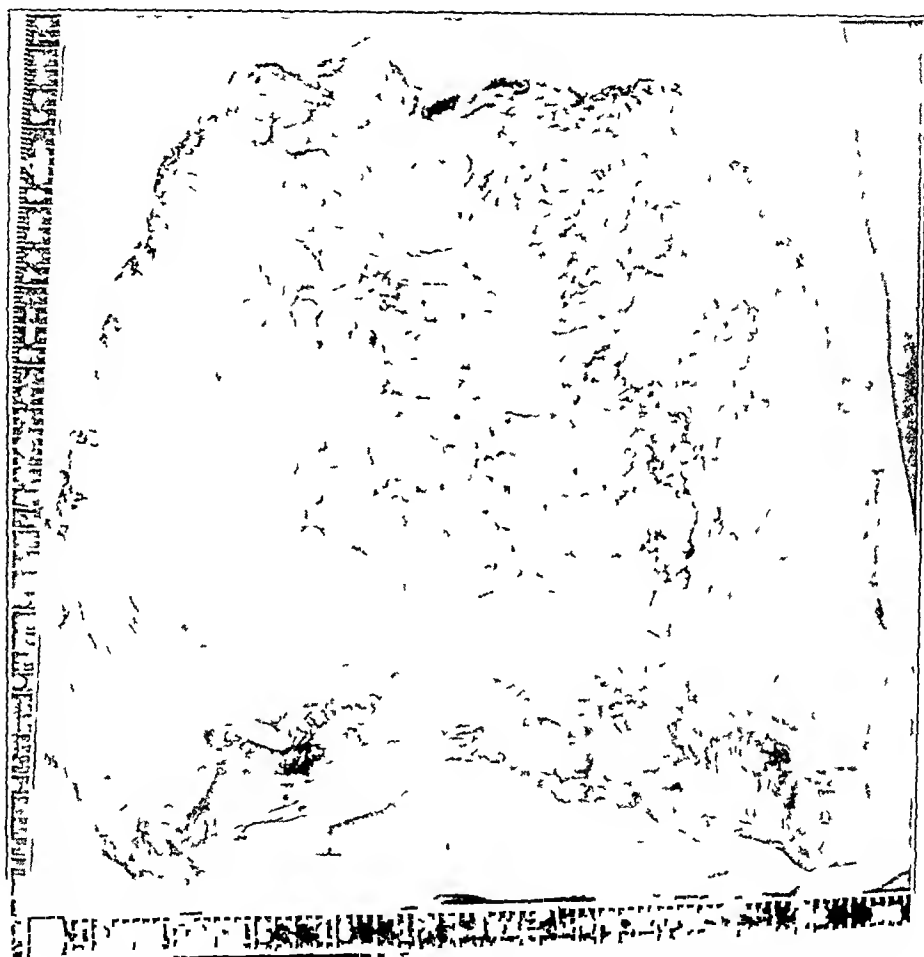


Fig 17 (case 12) —Same as figure 16, showing autopsy specimen of the lungs.

Hodgkin's disease affects only the lymph tissues, whereas Hodgkin's sarcoma may metastasize like carcinoma or sarcoma, in this case it metastasized to the lungs.

CASE 13—Mrs M C W, aged 69, was admitted to the Steiner Clinic on Jan 23, 1929, complaining of several pigmented masses on the right side of the face, general weakness and loss in weight. The present illness had begun when the patient noted a small black wart or mole on the right eyebrow, which was removed in 1926 with a salve. The physician told her the growth was a cancer. It returned later and was not benefited by the application of salve or plaster. Later another mass appeared just anterior to the right ear, extending down on the neck. The cervical glands became enlarged. The hemoglobin was 80 per



Fig 18 (case 13)—Melanoma of the face with metastases to both lungs



Fig 19 (case 14)—Recurrent carcinoma of the left breast with extension to the pleura and lungs

cent The urine was positive for melanin A roentgenogram of the chest showed widespread blood-borne metastases to both lungs

A diagnosis was made of melanoma of the face (malignant) with metastases to both lungs

Roentgen irradiation was given on January 26, 28 and 30 and February 28

The patient died on March 17, 1929 Autopsy on March 18 showed metastases to the lungs, liver and spleen

CASE 14—Miss E M R, aged 43, was admitted to the Steiner Clinic on Jan 13, 1927, complaining of an ulcerating mass on the anterior, left side of

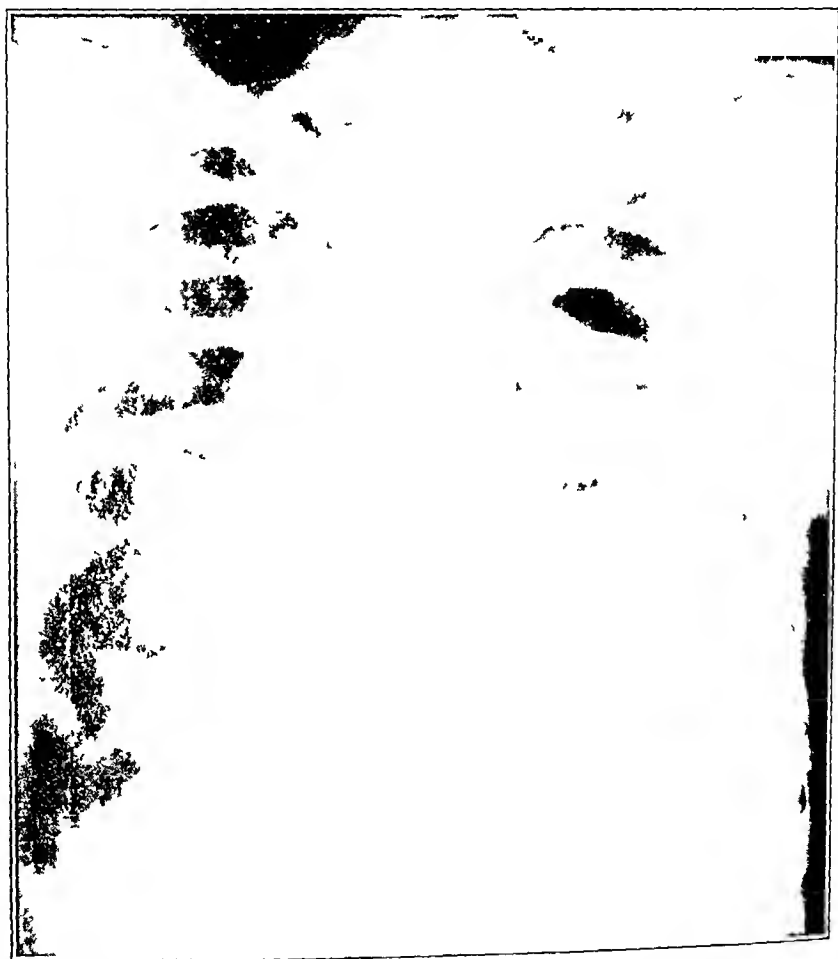


Fig 20 (case 15) —Secondary carcinoma of the lungs from a malignant teratoma of the right testicle

the thoracic wall The present illness followed an automobile accident in October, 1925, in which the patient's left breast was bruised A mass was noticed in December, 1925 She consulted a physician and was advised "to forget it" In October, 1926, the mass in the left breast was diagnosed as carcinoma At this time small glands were palpable in the supraclavicular space The breast was amputated Roentgen therapy was given both before and after operation

A roentgenogram on June 29, 1927, showed no evidence of thoracic metastases On December 30 a roentgenogram showed involvement of the intrathoracic structures, probably a direct extension from the local recurrence rather than a metastasis

A diagnosis was made of recurrent carcinoma of the left breast with direct extension to the pleura and possibly to the base of the left lung.

The patient died on March 25, 1928.

CASE 15.—A white male, aged 45, was admitted to my service at the George Peck Hospital on March 14, 1929, complaining of pains below the shoulder blades. The present illness began about three years before with swelling in the right testicle with some edema of the scrotum. At first there was no pain. Later sharp darting pains developed. Six months before admission was removed and sent to the laboratory for diagnosis. The report showed a teratoid tumor suggestive of malignancy. A few weeks following operation a mass developed in the right inguinal region and grew rapidly. Shortly afterward the patient noticed some difficulty in breathing, a feeling of fullness in the abdomen, some nausea and occasional vomiting. More recently sharp pains had developed beneath the shoulder blades and in the past month blood tinged sputum, some cough and frequent night sweats had been noticed.

Examination revealed a poorly developed and emaciated man. The right side of the chest was more prominent than the left with slight flaring on the left side on inspiration. Respirations were rapid and breath sounds were harsh and wheezy. There was a hyperresonance anteriorly in both apices while posteriorly the resonance was impaired and there was almost complete dullness. Moist rales were heard over the entire chest. The liver was enlarged and the spleen palpable. There was a tumor-like mass the size of an orange in the right inguinal region and the scrotum contained a large mass on the right side. The Wassermann reaction of the blood was 4 plus. The patient was mildly anemic. A roentgenogram showed multiple round opaque shadows varying in size from 1 to 6 cm in diameter throughout both lungs. There was a uniform dense shadow in the base of the right lung. A gland was removed from the groin. Microscopic examination showed teratoid tumor with carcinomatous changes.

A diagnosis was made of teratoid tumor of the right testicle malignant with carcinomatous metastases throughout both lungs.

The patient died on March 20, 1929. Autopsy confirmed the diagnosis.

### CONCLUSIONS

Intrathoracic tumors, both benign and malignant, are more common than was formerly supposed.

Benign tumors of the mediastinum and lungs often produce atelectasis and bronchiectasis by pressure.

Primary carcinoma of the lung and pulmonary tuberculosis may coexist in the same patient.

Abscess and primary carcinoma of the lung often coexist, and it is impossible to tell which is cause and which is effect.

Benign tumors of the chest should be removed surgically when accessible.

Roentgen therapy offers only palliative results in malignant neoplasms within the chest.

Early surgical intervention is the only hope for primary malignant growths within the chest.

In the treatment for intrathoracic neoplasms there should be a closer cooperation between the internist and the surgeon.

## ABSTRACT OF DISCUSSION

DR CARL A HEDBLUM, Chicago I quite agree with Dr Lilienthal that "benign" is not a good term for nonmalignant tumor, but if such a tumor injures health or shortens life, as it frequently does, the term nonmalignant seems to me preferable to "benign" or "innocent"

I should like to emphasize the importance of the early recognition of tumors of the lung and of the thoracic wall As Dr Lilienthal so well stressed in his presidential address in 1923, any advance in treatment under present methods is dependent on early diagnosis

We all agree, I think, that bronchoscopy is the most direct and the surest method of establishing the presence of bronchogenic tumor, but the diagnosis may be made not infrequently on biopsy of a hard cervical gland or of other superficial glands or tumors Occasionally clumps of malignant cells may be isolated from the sputum or from aspirated pleural exudate

In my opinion we should discriminate sharply between primary malignant tumors of the lung or the thoracic wall and those due to metastasis Metastases are common, as we all recognize, and signify, generally speaking, the same hopeless prognosis as metastasis elsewhere

I have performed exploratory thoracotomies on a number of patients with bronchogenic carcinoma, but in every case the tumor had infiltrated the hilus, Radium implants in such cases in my experience seemed to prolong life and to relieve symptoms I have drained abscesses secondary to tumor of the lung with marked palliative results In cases with marked retraction of the mediastinum from atelectasis secondary to occlusions of the bronchus by the malignant growth, phrenicectomy may give some relief of the symptoms In cases of indefinite tumors of the wall of the chest, early radical excision may be more conservative than waiting for a tumor to grow to such proportions that diagnosis becomes obvious but excision difficult or useless

DR WILLIAM A HUDSON, Detroit There is just one point in regard to the question of early diagnosis which I think cannot be emphasized too strongly It has occurred to us that the developmental period of tumors of the lung is much longer than we have heretofore considered We have now one case that has been under observation by numerous medical men over a period of seven years in which there was one symptom that was outstanding, and it was only after investigation of that particular symptom that a diagnosis was made That symptom was spitting of blood It recurred at irregular intervals throughout the period of observation Bronchoscopy was performed on this patient three years ago by ourselves, at which time an ulcerative lesion was found in the lower lobe of the left bronchus, the lesion was not characteristically cancerous, but was suggestive The patient was told at the time that it was a suspicious lesion, and that it should be kept under close observation One year later bronchoscopy was performed by Dr Clerf, who removed a specimen, and at the same time he told the patient that it was a suspicious lesion, but the specimen which was removed was reported as granulation tissue Six weeks later we again performed a bronchoscopy and were able to penetrate to the orifice of a tertiary bronchus from which a nodule was seen to protrude We removed a specimen smaller than my small finger-nail, removing practically the entire mass Microscopic studies confirmed the suspicion of carcinoma of the bronchus The patient has received radium and roentgen therapy and is still in good condition

We feel that the developmental period is much longer than we have heretofore considered, this case presenting symptoms extending over a period of seven

years. Is it not possible that the development of the tumors such as Dr. Davison has shown extend over a period of ten, fifteen or even twenty years?

DR. L. I. LEWALD, New York. On account of the difficulty of making a differential diagnosis of some of the mediastinal tumors, I will show two slides to illustrate it. (For a report and illustration of this case see *Röntgenologie*, Diagnosis of Thoracic Dermoids, *Arch. Surg.* 18:301 [Jan.] 1929.)

The tumor shown in the first slide occurred in a man aged 57 and was said to have given slight pressure symptoms and slight dyspnea. The question of whether it was an aneurysm or a mediastinal dermoid is the point that I wish to emphasize. In regard to the question of pulsation do not be misled by an apparent pulsation under the fluoroscope indicative of aneurysm. A tumor of this sort so closely related to the aorta and the heart will be lifted in such a way that one might believe that it showed pulsation. This tumor was examined by a number of roentgenologists, some of whom thought they saw pulsation. I first saw the case at the New York University Clinic and diagnosed it as mediastinal dermoid, having seen one other case of mediastinal dermoid in which the patient was afterward successfully operated on by Dr. Lahunthal (*Arch. Surg.* 18:303 [Jan.] 1929).

The patient in question spontaneously coughed up the tumor. It is rather interesting that in a similar case shown by Dr. Barker at the New York Academy of Medicine, a roentgenologist had diagnosed aneurysm and then showed a film like the second one presented, showing that the aneurysm had disappeared. The same thing happened in this case. Dr. Samuel Lambert obtained the final roentgenogram of this case for me at the Presbyterian Hospital two and a half years later. The patient entered the hospital at that time because of foul expectoration and a roentgenogram made at that time showed that the tumor had disappeared except for the sort of encapsulated appearance shown in the second slide. Dr. Lambert tried to trace the microscopic examination of the material that was coughed up, but was unable to find a report in the laboratory. His remark is that as the material was probably foul and possibly contained hair, it was thrown away as not being a satisfactory specimen. He reports it in his article on intrathoracic tumors as a mediastinal dermoid that suppurated and was evacuated in this way.

DR. HOWARD LAHUNTHAL, New York. I have often wondered about the mistaking of dermoids and tumors of that sort for aneurysms on account of the apparent expansile pulsation. There may be an excuse for such mistakes.

We do not look at the tumor merely on a plane, it is not merely pushed to the side by the heart, it may be pushed away from the observer and therefore become larger in all dimensions as it goes away from him and smaller in all dimensions as it approaches him, thus simulating a true expansile pulsation. I should like to know what Dr. LeWald thinks of this.

DR. L. T. LEWALD, New York. I think that this explanation sounds reasonable, however, I should like to see it proved in a series of rapidly made exposures in which one could study the phenomenon differentially rather than to trust to one's eye and the fluoroscope alone.

DR. T. C. DAVISON, Atlanta, Ga. It is hoped that an abstract of this discussion may be placed before the medical profession in order to stimulate increased interest in intrathoracic tumors, and to bring about a closer cooperation between the internist and the surgeon.



# REMOVAL OF METASTATIC CARCINOMA OF THE LUNG AND MEDIASTINUM

## SUGGESTIONS AS TO TECHNIC

FRANZ TOREK, M D

NEW YORK

*History*—Mrs C T, aged 42, had had a complete hysterectomy for carcinoma, performed by Dr Arthur Stein in May, 1927. The recovery was normal in all respects, except that a vesicovaginal fistula ensued. This was operated on by Dr Stein in August, 1927, and healed.

The patient remained well until August, 1929, when she began to complain of dysphagia, which by November became so much worse that she was no longer able to eat solid food. Her weight dropped from 105 pounds (47.6 Kg) in August to 90 pounds (40.8 Kg) in December. There was no history of pulmonary disease, no cough or pain in the chest. Occasionally, she felt her heart pound somewhat.

Roentgen examination on December 26 revealed a large, smooth, round, sharply circumscribed mass in the right portion of the chest, extending beyond the right border of the heart. It occupied the area of the eighth, ninth and tenth intercostal spaces and measured about 11 cm across. The lower half of the esophagus was displaced forward by the mass, being sharply angulated where it came in contact with the upper border of the tumor. At the diaphragm the tumor was pressed against the anterior part of the hiatus. The heart was also pressed forward. The stomach was ptosed, it showed a large six hour retention and a small twenty-four hour residue. The descending duodenum was the seat of a diverticulum. A vaginal and abdominal examination, made by Dr Stein, showed no local recurrence.

I saw the patient early in January, 1930. An examination revealed dullness low down on the posterior aspect of the chest, especially on the right side, on the left side there was also dullness, but here it was confined to an area close to the spine. The breath sounds over the dull area were faint, above that area the voice transmission was exaggerated. An occasional râle was heard here and there.

The patient's history pointed strongly toward the diagnosis of metastatic carcinoma of the lung. However, the outline of the new growth was so well defined that the roentgenologists as well as the physicians, including myself, considered the roentgen picture to be characteristic of a nonmalignant growth, probably a mediastinal dermoid. As is usual with dermoids in that location, the esophagus and the heart also, to some extent, had been displaced forward. This diagnosis seemed to be further supported by the fact that the gynecologist could find nothing suggestive of a local recurrence. Finally, there seemed to be no good reason for assuming that a patient who had had carcinoma should not also have a mediastinal dermoid.

Attempts were made at the hospital to feed the patient previous to her operation, but instead of gaining, she even lost weight during the attempt.

*Operation*—Operation was performed on January 20. I had planned to remove the supposed mediastinal dermoid extrapleurally, if possible. A posterolateral incision was made through the eighth intercostal space from the angle of the

rib to the midaxillary line, and a second incision was made from the posterior end of the first incision downward, corresponding to the ninth, tenth and eleventh ribs. The incision was carried down to the pleura but not through it. The parietal pleura was separated from the eighth and ninth ribs, well forward beyond the anterior end of the incision and well backward to the spine. Then it was loosened down to the diaphragm. In the course of this procedure, the ninth, tenth and eleventh ribs were cut about at their angles, as soon as each one had been separated from its parietal pleura. It soon became apparent that the mass was a tumor of the lung which had extended into the mediastinum and had become firmly attached to its surroundings, especially at the diaphragm and the vertebrae. The dissection was nevertheless continued extrapleurally, since thus the likelihood of remaining outside the involved area was enhanced and the lung could retain its normal covering of parietal pleura for a maximum amount of



Fig 1—Tumor of the lung and mediastinum. The tumor occupies an area from the eighth to the tenth intercostal space inclusive and measures 11 cm across. It is for the most part on the right side and has pushed the esophagus forward, causing obstruction which is most marked at the hiatus, where the esophagus could not yield so well to the pressure of the tumor.

time. Finally, the last step in the resection, that of cutting the tumor off the lung and of properly caring for the cut surface, could be done best when the new growth required no further care and when the operator's attention could be centered on the only surface from which bleeding was still to be expected. There was some spurting from the cut surface of the lung, which was caught without much difficulty and the raw surface was later closed by a continuous catgut suture. The pleura was then sutured wherever possible, but this could be done only partially, because portions of it had to be sacrificed in the removal. The lung was then inflated, and the wound closed without drainage, using two pericostal sutures of chromic catgut to approximate the eighth and ninth ribs, chromic gut for the muscles and silk for the skin. After the patient had been brought back to her room, she was given a blood transfusion of 500 cc.

*Course*—The wound healed without any disturbance. As I was uncertain whether the wound in the lung had been closed air tight, frequent examination was made the first few days for the presence of a mediastinal emphysema, but none occurred. A pleuritic exudate of moderate extent, on the right side, which gave rise to no subjective symptoms, was noted after the operation and had not been completely reabsorbed after six weeks. It has since disappeared. A roentgenogram taken about that time showed the absence of the tumor. The esophagus was more nearly straight but not properly filled, which latter condition was believed to be ascribable partly to adhesions, partly to spasm invoked reflexly by

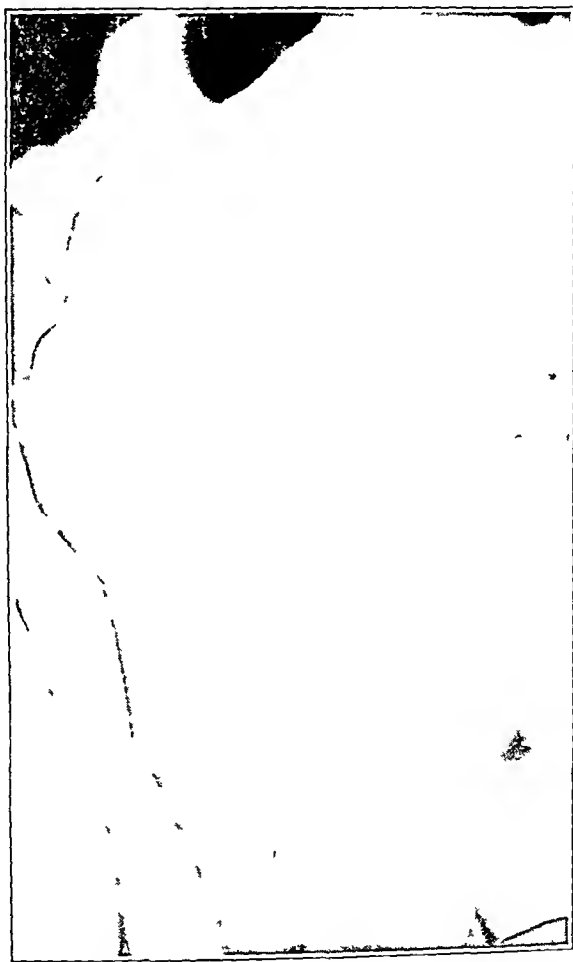


Fig 2—The patient after the wound had healed, showing the incision which goes through the eighth intercostal space, with an extension from its mesial end downward over three ribs which were divided.

the duodenal diverticulum with the twenty-four hour residue in the stomach. At any rate, the patient had for some time been able to eat meat, vegetables, bread etc., provided she ate slowly.

*Pathologic Report*—The tumor was composed of a thin, interlacing stroma in which was soft, friable, almost gelatinous tissue. The tumor was vascular and several areas of diffuse hemorrhage were seen in its substance. Sections of the peripheral portions showed a carcinoma composed, for the most part, of columnar and islands of pavement epithelium supported by delicate strands of fibrous tissue bearing this epithelium with blood vessels of small caliber. The greater part of

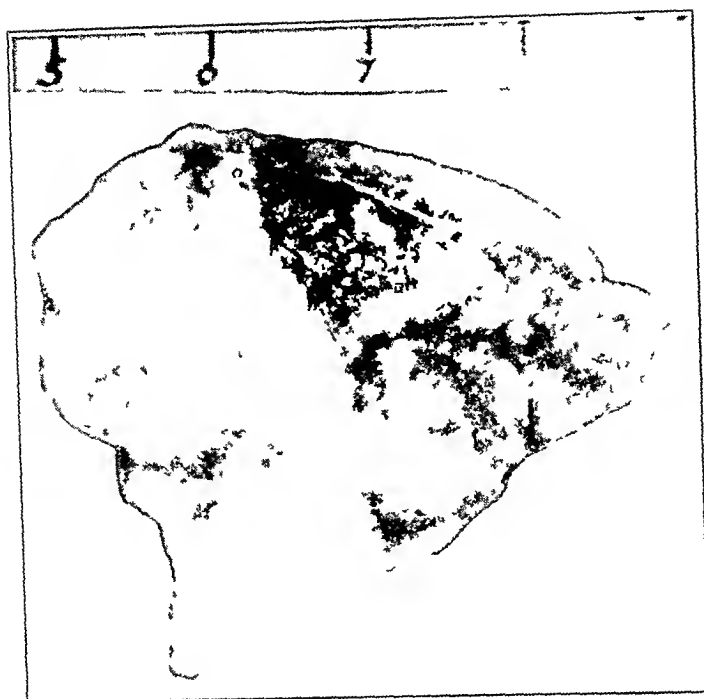


Fig 3—The tumor



Fig 4—Photomicrograph of the adeno-acanthoma

the epithelium showed neither intercellular bridges nor epithelial pearls. The constituent cells were usually small and hyperchromatic, though there were areas composed of larger cells which stained less deeply with hematoxylin. Mitotic figures were fairly numerous. In many areas there were small masses of nests of differentiated squamous epithelium often showing central cornification or pearl formation. Included in the tumor were a few small spaces bordered by cylindric epithelium or more or less well defined glandular acini. Near one surface of the tumor there were small islands of pulmonary tissue, and attached to the surface was a small amount of atelectatic lung tissue. Toward the deepest part, the tumor showed extensive necrosis, sometimes with replacement fibrosis. In the newly formed fibrous tissue were a number of cholesterol crystal spaces, often bordered by giant cells. A diagnosis of adeno-acanthoma of the lung and posterior mediastinum, secondary to adeno-acanthoma of the uterus was made.



Fig 5—Roentgenogram after removal of the tumor. The esophagus has straightened out considerably but is still somewhat out of shape, due probably to adhesions.

#### COMMENT

As the tumor was a metastatic one, this history is, of course, not presented as that of a case in which cure was obtained. Metastases are more likely to be multiple than solitary, and I saw some enlarged lymph nodes at the right bronchus but did not take any out for examination, as a prolongation of the operation did not seem warranted. There is, possibly, one brighter side to the case in the fact that uterine carcinomas are fairly radiosensitive and that this carcinoma of the lung is identical in type with the original uterine new growth. Working on this hypothesis, the patient has already received two series of deep Roentgen treatments and is at the present time back in the hospital for a third series.

The case is of interest because it offers a few topics for consideration. In the first place, there is the question of the permissibility of operating at all in the case of a metastasis. Frankly, I must admit, that had I known positively that the tumor was a metastasis, I doubt that I would have had the courage to operate. I operated under a wrong diagnosis, with the rather unexpected result that the patient is thankful to me for doing so. Now, having had this experience, I should not be inclined to be too dogmatic in refusing to remove a metastatic new growth. In this case, the tumor caused obstruction of the esophagus, and that fact, I think, was sufficient reason for removing the tumor. One should, I believe, be guided by the indications in each case and not take a hard and fast stand for or against the removal of a metastatic new growth.

In the second place, the technic might deserve consideration, not simply in its application to this particular case, but also in its application to primary tumors of the lung. In some of these primary carcinomas the extrapleural approach may perhaps be of advantage, provided the tumor is situated near a margin or corner of the lung. The customary attack is intrapleural, and in the course of it, one frequently encounters firm adhesions binding the affected lung to the parietal pleura. If the resection is made outside of these adhesions, extrapleurally, the likelihood that one is proceeding in unaffected tissue is greater than if these adhesions are divided intrapleurally.

In the third place, although even with an intrapleural approach it is feasible to excise the aforementioned adhesions of a carcinoma of the lung together with their parietal pleura, this extrapleural method has the additional advantage of permitting the lung to remain protected by the best possible covering, its own pleura, for a maximum length of time, thus reducing to a minimum the irritation of its surface, to which it would otherwise be subjected by pads, hands and other foreign material. Grave of Moscow claimed that irritation of the terminal sensory vagus filaments of the lung caused "vagus pulse" and disturbance of respiration. The retention of the parietal pleura as long as possible would undoubtedly reduce any possible vagus irritation from that source.

#### ABSTRACT OF DISCUSSION

DR. WILLY MEYER, New York. As far as therapy is concerned, bronchoscopy is a close running mate with surgery in many conditions of the lung. We have seen and heard again this morning—and we all know it from our own personal experience for years—that many bronchiectatic conditions and abscess of the lung can be cured by bronchoscopy and bronchoscopic treatment. If the bronchoscopist is strict in his self-criticism and after a certain time is ready to say,

"I am at my wits' end, now this case will go to the surgeon," the patient will have been done full justice. The same can be said about other diseases of the lung. After all, the saving of life is the principal point in medical and surgical

treatment, we know that the danger from bronchoscopy and intrabronchial treatment is much less than that from an operation. If science can possibly help a patient with milder means, often permanently, this should be tried first.

Regarding cancer of the lung, we know that in at least 90 per cent of the cases the trouble starts in the main bronchus, principally in the right. What does such a patient show clinically, who is afflicted with a beginning cancer of the bronchus? He has principally the inclination to cough, a cough that cannot be explained, because no pathologic condition is found by the internist, and nothing is shown at that early time by roentgenographic examination. If the attending physician is progressive and properly trained, he will soon consider bronchoscopy, suspecting perhaps a malignant tumor in the bronchus, suspicion of the presence of a foreign body being unfounded. And if the specialist finds an irregularity of the surface of the bronchial mucosa, he will make a biopsy and let the pathologist tell him the diagnosis.

Regarding the value of a therapeutic proposition in medicine, I have always believed that if two minds have had the same idea about the treatment for some trouble, independently, there is likely something useful in what they are proposing. By chance, I read a paper before our Association on cancer of the lung two years ago. While working on it, I wondered whether one should not, if the condition were definitely diagnosed, attack that small, beginning tumor of the bronchus at once as radically as possible, namely, thoroughly burn it away with actual cautery. With this in mind, I went to the attending laryngologist and bronchoscopist of our hospital, Dr. John D. Kernan. I said to him, "Dr. Kernan, can you invent or construct an instrument which, introduced through the bronchoscope, will permit you to thoroughly cauterize that place in the wall of the bronchus, from where you took the biopsy, which permitted the pathologic diagnosis?"

He smiled and said, "Doctor, I have done that already."

A report of his case has not been published so far. The gist of the matter is that an early cancer definitely diagnosed by the pathologist from a biopsied specimen was thoroughly cauterized through the bronchoscopic tube, and was also treated later on with gold radon implants introduced and placed through the tube, and the patient, a woman, was cured, and was still cured when I last heard of her through Dr. Kernan a few days ago.

A second case, also that of a patient of Dr. Kernan, is on record. The fact is that Dr. Kernan had the primary idea, and that I had the same, independently. Such occurrence would have been some firm basis for action on these lines even if we were not yet in possession of two cases of early cancer in which cure appeared to be obtained in this way. Besides making the correct diagnosis, the point worth emphasizing is the actual cauterization. The more intensive the local reactive hyperemia produced, the greater is the hope for a radical cure.

Why is it that a cancer of the lung starts in the bronchus so frequently and not in the parenchyma? Because, we believe, the careful analysis of the development of cancer shows that a cancer, not only of the lung, but of any organ, develops with predilection in places generally where there is more rest, and in that part of the same organ which is least active. On the other hand, where there is much motion, viz., active hyperemia, i. e., strong circulation due to the activity of the organ, there occurs rarely, if at all, the formation of cancer.

A few years ago, at one of the annual meetings of the American Association for Cancer Research, a member, speaking of the subject of chronic irritation, said, 'If one could but explain why the breast of a farmer's milk cow, that is

so battered and maltreated by the calf and not only by the calf but by the oldtime process of milking day after day, hardly ever becomes the seat of a cancer." A few years later, being engaged in studies on the genesis and on the development of cancer, I ventured to give the explanation just mentioned. The heart muscle, at work day and night, is very rarely the seat of primary cancer. We eat three times a day, six hours is the longest time the food stays in the stomach, from there it passes on at brief intervals into the duodenum stimulating it to almost continuous activity. With four large-sized arteries feeding the area with blood, the duodenum rarely harbors a cancer. Of course, we know that chemistry likely also plays a role in the etiology.

Coming back to the subject of cancer of the lung, I am absolutely convinced that if we all band together, at least the members of our Association, and impress on our confreres that a patient with a persistent unexplained cough must be given a bronchoscopic examination, and if the bronchoscopist takes a specimen by means of biopsy and the pathologist finds it malignant, with early removal with the wire sling, if pedunculated, and thorough cauterization with subsequent treatment along conservative lines, the terrible hardship for patients with cancer of the lung will gradually disappear and more cases of a permanent cure of cancer of the bronchus placed on record.

Years ago I had a patient with a large intrathoracic pulsating tumor, it made the entire chest pulsate and did not have the earmarks of a typical aneurysm. It was hard to explain. On exploratory thoracotomy, an enormous distention of the entire aorta, a massive total aortic aneurysm, was found. It began at the arch of the aorta and went down to the space where the vessel passes through the diaphragm. Nothing could be done surgically. I closed the thorax, and the patient recovered so far as the operation was concerned. The case proves, that even in such dangerous cases of pathologic processes, the body stands an exploratory thoracotomy very well. Today we know that exploratory thoracotomy is no more dangerous than exploratory laparotomy. Why then not, when one sees on the x-ray plate an intrathoracic tumor and the patient is suffering, make an exploratory thoracotomy and see whether we can bring help?

I wish to congratulate Dr. Torek that he went ahead in this case and had success.

DR. POL N. CORYLLOS, New York. I want to congratulate Dr. Torek on reporting his error in the diagnosis of the metastatic character of this tumor, which led him to such excellent operative success and gave us the opportunity to hear about this unusual case. It is the first case, to my knowledge, of an operation on a secondary carcinoma of the lung. This shows that in cases of metastatic tumor of the lung, complicated by compression of the intrathoracic organs endangering the life of the patient, a radical procedure is perfectly legitimate. It shows, furthermore, that the distinction between tumors of the lungs as benign, malignant or whatever else one may wish to call them has no practical significance. There is no such thing as a "benign" or even an "innocent" tumor of the lung or of the thoracic cavity, if such tumor is liable to increase in size. A time inevitably comes when by its mere growth it produces by compression complications jeopardizing the life of the patient. I should suggest to differentiate tumors by the terms 'operable' and "inoperable," and to operate on them first and leave the laboratory to determine afterward their exact nature and grade of malignancy.

I am in perfect accord with the opinion of Dr. Torek concerning the great advantages of the extrapleural approach. Yet if the lung is free from adhesions,



I do not think there are many advantages in using this method. A preliminary, artificial pneumothorax, by allowing us to estimate the existence or absence of pleuropulmonary adhesions, would give some valuable indications as to the procedure to follow.

Another remarkable point in this case is the facility with which the tumor was enucleated. This shows once more that in thoracic surgery, especially for tumors of the lung, well measured boldness is of great value.

## PROCEEDINGS

SUNDAY, MAY 11

The Council met in an executive session at 8 p m

MONDAY, MAY 12

A dry clinic was given by the staff at the Jefferson Hospital at 9 a m

The meeting convened at 2 p m at the College of Physicians, Mitchell Hall

The following papers were read

Dr Edgar W Phillips, Rochester, N Y "Hydatid Cysts of the Lung  
Review of the Recorded North American Cases"

Dr Stuart W Harrington, Rochester, Minn "Amebic Hepatic, Subphrenic  
and Pulmonary Abscesses"

Dr Howard Lilienthal, New York "Giant Sarcoma of the Pleura Report  
of Two Cases with Remarks on Operative Exploration of the Thorax"

Dr T C Davison, Atlanta, Ga "Intrathoracic Tumors Report of Cases"

Dr Franz Torek, New York "Removal of Metastatic Carcinoma of the  
Lung and Mediastinum Suggestions as to Technic"

Dr Claude S Beck and Dr R A Griswold, Cleveland "Pericardiectomy in  
the Treatment of the Pick Syndrome Experimental and Clinical Observations"

TUESDAY, MAY 13

Demonstrations of methods of the technic and of experimental work were  
given by the staff of the University Hospital at 9 30 a m

The Council met in executive session at 1 p m

The meeting convened at 2 p m at the College of Physicians, Mitchell Hall  
The Association met in executive session for the election of officers, new members  
and such other business as was brought before the meeting

The following papers were presented

Dr Wyman Whittemore, Boston President's Address, "Exploration of the  
Pericardium and Decompression of the Heart Report of Case"

Dr Carl A Hedblom, Chicago "Anterolateral Costectomy for Inadequate  
Collapse Following Posterior Extrapleural Thoracoplasty"

Dr Frank B Berry, New York "The Unfavorable Results of Phrenicectomy"

Dr E J O'Brien, Detroit "Collapse Therapy Reasons for and Mechanisms  
of the Therapy with Deductions Based on Observations of Seven Hundred  
Patients"

Dr Francis A C Scrimger, Montreal, Canada "Idiopathic Dilatation of the  
Esophagus"

Dr H C Ballou, Dr H M Wilson (by invitation), Dr J J Singer and  
Dr E A Graham, St Louis "Esophagus, Stomach and Heart Following  
Unilateral Phrenicectomy"

Dr Duff S Allen, St Louis "The Treatment for Penetrating Wounds of  
the Pleural Cavity"

President's Banquet was held at the Masl and Wig Club, University of  
Pennsylvania at 7 p m

WEDNESDAY, MAY 14

The meeting convened at 9 30 a m at the College of Physicians, Mitchell Hall The subject of promotion from active to senior membership was discussed

The following papers were read

Dr David T Smith, Ray Brook, N Y "Etiology of Primary Bronchiectasis"

Dr John H Gibbon, Jr (by invitation) and Dr Edward D Churchill, Boston  
"Changes in the Pulmonary Circulation Induced by Experimentally Produced Arteriovenous Fistula"

Dr C M Van Allen, Peiping, China, and Dr G F Lindskog, New Haven, Conn  
"Obstructive Pulmonary Atelectasis Problems of Pathogenesis and Clinical Management"

Dr Pol N Coryllos and Dr George L Birnbaum (by invitation), New York  
"Atelectasis of the Lung Rôle of Alveolar Gas Exchanges in Its Production"

## REPORT ON THE ACTIVITIES OF THE CHEST TUMOR REGISTRY

During the past year, the recommendations of the Council of the Association relative to the preparation and circulation of special blanks for the registration of chest tumors have been carried out. Several hundred of these blanks have been sent out, and the response has been gratifying. At present, the Registry contains records of about 100 cases. We have also received replies to a circular letter sent to members of the Association which contain promises of submission of at least 50 additional cases.

The Registrar has answered numerous inquiries concerning the Registry from surgeons throughout the country who are not members of the American Association for Thoracic Surgery, and blanks have been sent out for the registration of their cases. In addition, we are corresponding with several foreign clinics and hope to be able to obtain records of a considerable number of chest tumors from them.

Respectfully submitted,

WILLIAM DEW ANDRUS, Registrar

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## CHANGES IN CONSTITUTION AND BY-LAWS

At the Thirteenth Annual Meeting of the American Association for Thoracic Surgery, Article VII, Section 7 of the By-Laws was amended to read as follows:

In printing and publishing the annual transactions of the Association, it will incur expenses not to exceed \$60 for each article. If the cost for printing and illustrating any article exceeds this sum, the excess shall be charged as a special assessment against the author concerned."

# LIST OF MEMBERS OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY 1930

## Honorary Members

Dr Edward R Baldwin	6 Church Street, Saranac Lake, N Y
Dr Alexis Carrel	Rockefeller Institute for Med Res, New York
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tion, great care had to be exercised not to rupture the axillary artery or the brachial plexus or fracture the humerus. When the head of the humerus was brought to the anterior border of the glenoid, and the arm was immobilized with the hand on the opposite shoulder, spontaneous reduction often occurred.

*Chronic Recurring Temporomaxillary Subluxation* — MORRIS<sup>65</sup> described carefully the intricate anatomy of the temporomandibular joint and discussed the mechanics and pathology of "snapping jaw." He advised operative correction of this condition rather than the use of external or intra-oral splints, such as had been advocated by some writers. Two operative procedures were suggested: (1) Nieder's operation which consisted of turning down a flap of temporal fascia and sewing the end to the capsule of the joint so as to limit the excursion of the condylar head, and (2) the procedure employed by MORRIS in which the condylar head was scarified and a series of reefing stitches was placed in the capsule.

*Habitual Dislocation of the Patella* — BLENCKE<sup>66</sup> discussed the various operations for the correction of habitual dislocation of the patella and stated that during recent years he had used a modification of the operation described by Drehmann. This consisted of transplanting the insertion of the gracilis muscle into the outer border of the patella. The patella was displaced inward as much as possible, and the tendon was fixed subperiosteally under moderate tension. The leg was placed in splints for three weeks, after which exercise and massage were begun. After four weeks the patient was permitted to walk, and a week later he was allowed to leave the hospital wearing an elastic knee-cap. All of the patients on whom the operation had been performed remained free from recurrence, in spite of the fact that one sustained a severe traumatism to the leg five years after operation.

#### AMPUTATIONS

*The Healing of Amputated Bones* — BARBER<sup>67</sup> studied the amputation stumps in forty skeletons, and observed the successive changes that took place in the process of healing and repair of the end of the bone. Briefly, these changes were found to be comparable to those of healing fractures. These in order were: (1) vascular erosion of the end of the bone and the adjacent shaft, (2) macular disintegration of the bone adjoining the site of amputation, (3) rounding of the bony stump, (4) closure of the medullary cavity by a cap of bone which rapidly became condensed and (5) restrained production or absence of osteophytes.

<sup>65</sup> Morris, J. H. *Surg. Gynec. Obst.* 50:483, 1930.

<sup>66</sup> Blencke, B. *Zentralbl. f. Chir.* 57:1159, 1930.

<sup>67</sup> Barber, C. G. *Ann. Surg.* 90:985, 1929.

The formation of the osteophyte on the femur was usually harmful, whereas on the tibia or the fibula it frequently caused union between the two and was to be desired

#### RESEARCH

*The Bacteriology of Normal Bone*—Santos<sup>68</sup> made bacteriologic studies of twenty-four specimens of bone and marrow obtained from persons without bone lesions and of twenty-four samples of bone obtained from apparently healthy dogs. No organisms were recovered from any of these samples. The author considered that this was corroborative evidence that the streptococci and staphylococci that had previously been reported as recovered at times from solitary bone cysts were causally related to these bone lesions.

*The Stimulation of Bone Growth by Venous Stasis*—The effect of venous stasis on the growth of bone as indicated by the healing of fractures was studied experimentally by Pearse and Morton.<sup>69</sup> In twelve dogs, portions of the fibula of identical size were removed subperiosteally from both legs. On one side the popliteal vein which received the drainage from the fibula was ligated just distal to its confluence with the femoral vein while the other leg was used for control purposes. The repair of the bony gap was observed by periodic roentgenograms. It was found that the union was accelerated on the ligated side in every case except one in which an interposition of muscle had occurred. In two patients who showed markedly delayed union of fractures, callous formation occurred promptly after the induction of intermittent venous stasis with a blood pressure cuff inflated a little above the level of diastolic pressure.

*The Effect and Mode of Action of Vitamin D*—Bauer and Marble<sup>70</sup> offered experimental evidence that the action of viosterol was to increase the absorption of calcium from the gastro-intestinal tract. They fed twelve cats on a diet deficient in calcium over a period long enough to reduce markedly the trabeculae in the bones. They then amputated the left fore leg of each cat. The animals were then placed on a high calcium diet, and six of the twelve cats were given viosterol. The animals were killed in pairs (one which had been given viosterol and one which had not). At varying lengths of time the humerus of each animal was studied. The humeri of the cats receiving viosterol showed a much greater increase in bone trabeculae than did the controls. Bauer and Marble were able to duplicate these observations with their clinical patients, as evidenced by complete calcium metabolism studies.

68 Santos, J. V. *J. Bone & Joint Surg.* **12** 150, 1930.

69 Pearse, H. E., and Morton, I. J. *J. Bone & Joint Surg.* **12** 97, 1930.

70 Bauer, W., and Marble, A. *New England J. Med.* **201** 809, 1929.



From experiments on guinea-pigs, Roi<sup>71</sup> believed that the administration of viosterol accelerates the processes of repair and the consolidation of the callus. He considered that the varying results obtained in experimental work depend on the type of irradiation used.

Brougher<sup>72</sup> studied the effect on the blood coagulation time of cod liver oil or viosterol in fourteen patients who showed a marked lowering of the blood coagulation time owing to various diseases. Viosterol was given in 10 drop doses and cod liver oil in doses of 30 cc. Four hours after cod liver oil or viosterol had been given, the clotting time was determined. In all instances it was found to be normal.

*The Influence of the Withdrawal of Blood on the Healing of Fractures*—Rallo<sup>73</sup> made a study of the influence of withdrawals of blood on the healing of fractures in rabbits. He found that periodic removals of a considerable quantity of blood resulted in an acceleration of the repair of fractures and increased the capacity for fixation of lime salts in all the tissues that were destined for this fixation.

*The Study of Semilunar Cartilages*—Tobler<sup>74</sup> made an examination of 400 semilunar cartilages obtained from 100 cadavers varying in age from infancy to old age. Beginning with the second decade, he found regularly evidences of different types of degeneration of the cartilages. Fatty degeneration was the most common, being found in 67 per cent, and mucous degeneration was noted in 15 per cent. After the thirty-seventh year all of the cartilages were found to show some signs of mucous degeneration. Almost as frequent as the mucous degeneration was what the author called asbestos-like degeneration. Incrustation of the degenerated areas with lime salts was seen in 25 per cent of all cases. The author considered the poor circulation of the semilunar cartilages responsible for the tendency to degeneration.

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71 Roi, G. *Riforma med* **45** 1551, 1929.

72 Brougher, J. C. *Northwest Med* **29** 38, 1930.

73 Rallo, A. *Riforma med* **45** 1345, 1929.

74 Tobler, T. *Schweiz med Wchnschr* **59** 1359, 1929.

## TUBERCLE-LIKE STRUCTURES IN HUMAN GOITERS\*

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In the routine microscopic examination of goiters removed at operation, one occasionally finds small nodules which are composed of epithelioid cells and giant cells. These nodules occur in the diffuse enlargements of the gland as well as in the circumscribed, nodose hyperplasias. In the nodose goiters they may be located in the nodes or outside in their vicinity in which location they are most frequent. A considerable literature has been devoted to the nodules and because of their morphologic similarity to miliary tubercles they are usually considered as such. In the older literature on the morbid anatomy of the thyroid gland, tuberculosis is described as being rare. Rokitansky never saw tuberculosis of the thyroid, and according to Virchow no other gland is as seldom affected by tuberculosis as is the thyroid. In miliary tuberculosis, however, the thyroid frequently is the site of tubercles which do not differ from the tubercles in other organs except that tubercle bacilli are scanty (Fraenkel<sup>1</sup>). In the chronic forms of tuberculosis, involvement of the thyroid unquestionably is rare. Thus, in ninety-four cases of chronic pulmonary tuberculosis, Chiari<sup>2</sup> found tubercles in the thyroid only four times (4 per cent). Hegar<sup>3</sup> examined the thyroid in 1,563 autopsies on tuberculous patients. He saw microscopic evidences of tuberculosis in only 0.4 per cent. This excludes cases of acute miliary tuberculosis. The infection of the thyroid with the tubercle bacilli may take place by way of the blood stream or lymph stream or by way of an adjacent tuberculous organ.

Contrary to the dead house experience of a relative immunity of the thyroid to tuberculosis which seems to be supported by some experimental observations, tubercles in goiters from patients with no other signs of an active tuberculosis have frequently been described. In practically all of the cases the tubercles were observed incidentally. The patients recovered quickly from the operation and if followed over a sufficient length of time were found not to show any other signs of

\*Submitted for publication, March 13, 1930.

<sup>1</sup> From the Department of Pathology of the Cook County Hospital and the Uihlein Memorial Laboratory of the Grant Hospital.

<sup>1</sup> Fraenkel E. Virchows Arch f path Anat 104 58 1886

<sup>2</sup> Chiari, H. Wien med Jahrb 69 119 1878

<sup>3</sup> Hegar. Inaug Diss, Kiel 1891

tuberculosis The frequency of this so-called "benign tuberculosis of the thyroid" varies In a material of 1,200 goiters, Collier and Huggins<sup>4</sup> saw tubercles five times (0.4 per cent) In 90 cases Marcuse<sup>5</sup> observed 2 tuberculous goiters In Smith and Leech's<sup>6</sup> series of 1,500 goiters, there were 3 with tubercle-like nodules (0.25 per cent) In Uemura's<sup>7</sup> statistics, which are based on 1,400 goiters, the frequency of tuberculous changes is given with 1.7 per cent, while Werdt<sup>8</sup> found them three times in 144 cases of simple goiter (0.25 per cent) and once in 28 cases of exophthalmic goiter

The majority of the authors state that the tubercles of the goiters are located in the stroma and in the follicles The tubercles consist of epithelioid cells which are often surrounded by a zone of lymphocytes There is a varying number of giant cells which are usually of Langhans' type Caseation is rare, and if present is insignificant The nodules are embedded with much dense fibrillar connective tissue, and it is this fibrosis that causes the firmness of the gland that makes one suspicious of a malignant tumor

Few of the investigators were successful in demonstrating acid-fast bacilli in the lesions, if present, they were scanty According to Hedinger,<sup>9</sup> dissolving of the gland with antiformin greatly facilitates the detection of the micro-organisms, but Mosiman<sup>10</sup> complained that the acid-fast granules and shrunken structures obtained by this method are difficult to identify as tubercle bacilli Most of the authors, therefore, resort to the histologic picture as sufficient proof of the tuberculous nature of the condition, believing that the benign character of the lesion is due to the low virulence of the bacilli or to infections with such small numbers of bacilli that they escape microscopic observation, or that the lesion is not the result of the tubercle bacilli themselves but of toxins liberated in some other parts of the body

The fact that the clinical history often shows no signs of tuberculosis in spite of the changes in the thyroid, which sometimes are rather extensive, and the failure to demonstrate the micro-organisms cast doubt on the tuberculous nature of many of the cases of so-called benign tuberculosis of the thyroid It is the purpose in this paper to show that in the thyroid may occur nontuberculous lesions that are similar to tubercles In a material of 300 goiters these changes were recorded four times

4 Collier, A., and Huggins, C. B. *Ann Surg* **84** 804, 1926

5 Marcuse, E. *Med Klin* **24** 775, 1928

6 Smith, L. W., and Leech, J. V. *S Clin North America* **8** 185, 1928

7 Uemura, S. *Deutsche Ztschr f Chir* **140** 242, 1917

8 Werdt, V. *Frankfurt Ztschr f Path* **8** 401, 1911

9 Hedinger, E. *Deutsche Ztschr f Chir* **116** 124, 1912

10 Mosiman, R. E. *Surg Gynec Obst* **24** 680 1917

## REPORT OF CASES

CASE 1—*History*—A student nurse, aged 22, showed clinical symptoms of a mild thyrotoxicosis of one year's duration. The basal metabolic rate was plus 25. The history was negative for tuberculosis. Physical and roentgen examination of the chest gave negative results. Partial lobectomy was performed. The portion of gland that was removed contained several nodes from 1 to 5 mm in diameter, which were rich in colloid. The intervening thyroid tissue was very firm and a light grayish brown.

*Microscopic Examination*—The gland contained many nodules that were surrounded by thick capsules of fibrillar connective tissue. The smaller nodules were composed of small follicles which contained little colloid and were lined by a high cylindric epithelium. The larger nodules were made up of medium-sized and large follicles filled by thick colloid and lined by a flat epithelium. In places the epithelium was thrown up to short papillary infoldings and assumed cuboidal or cylindric shape. Outside the nodules the thyroid showed a lobular structure, the lobules being separated by a varying amount of fibrillar connective tissue. The majority of the lobules were formed by medium-sized, colloid-filled follicles with a low cuboidal lining. Some of the lobules contained follicles of irregular shape in which the colloid was replaced by a pale-stained material. The lining was cuboidal or cylindric, with an occasional papillary infolding. Here and there the lumen of a follicle was filled with desquamated round or oval cells which had an ample oxyphilic cytoplasm and light-stained, round or oval nuclei. These cells sometimes fused together into a single protoplasmic body from which fine processes extended to the epithelial lining.

A striking feature was the presence in the stroma of numerous well defined and sharply circumscribed nodules. These nodules, which were composed of light-stained cells, were scattered throughout the gland but were not found inside the nodules formed by the modified thyroid tissue. The nodules lay single or in groups, the largest of which had the size of a lobule. The groups were surrounded by much fibrillar connective tissue, which was connected with the stroma. In the periphery or in the center there was often an accumulation of lymphocytes (fig 1). The cells of the nodules possessed an ample oxyphilic cytoplasm. Their shape was oval, and their nuclei contained a scanty, finely granular chromatin net and one or two distinct small nucleoli. There were many cells with multiple nuclei arranged peripherally about a homogeneous or finely vacuolated center. The nuclei showed the same structure as in the cells with a single nucleus.

Connective tissue stains, in particular Mallory's aniline blue stain, demonstrated about the nodules a capsule of fibrillar connective tissue. This capsule contained blood capillaries which encircled the nodules much as they did the follicles. The connective tissue fibrils did not extend inside the nodules. The Mallory stain also brought out another interesting feature, namely, the presence between the epithelioid cells of a substance that stained a bright orange yellow or red, as did the colloid in some of the follicles. The substance appeared as deeply indented, drawn out or lancet-shaped bodies, which were wedged in between the cells or enclosed in a large multinucleated cell.

A study of the slides revealed transitional stages between the follicles and the cellular nodules of the stroma (figs 2 and 3). The swelling and desquamation of the follicular epithelium already described were the initial stage. Later, the lining epithelium showed the same structural changes as did the cells living free in the lumen. Some of the cells fused together to form giant cells. The follicle

filled by the large oxyphilic cells and by giant cells resembled a young tubercle. There was still the layer of fibrillar connective tissue with the characteristic arrangement of the capillaries about the nodule, and there were still the debris of inspissated colloid between the cells, indicating the origin of the nodules from follicles. The picture later became more complicated by fibrillar connective tissue growing into the nodules and replacing them more and more. Thus, finally



Fig 1 (case 1) —A group of fully developed nodules surrounding a center of lymphoid tissue. There are many epithelioid cells and giant cells. In the periphery single follicles are seen taking part in forming the nodules. The nodules are surrounded by fibrillar connective tissue. The whole area represents a lobule.

there was a dense scar which passed into the increased interstitial tissue. Lymphocytes may take part in the transformation of the follicles, though their share is limited.

Caseation could not be observed, and the most careful search for tubercle bacilli in thin and thick sections and in anti-formin-treated material was negative.

The transformation of follicles into tubercle-like nodules may affect both fully developed, mature follicles and small and newly formed ones. The nodules resulting from the young follicles are small, and since these young follicles lie close together, separated only by a scanty stroma and capillaries, a group of transformed follicles may appear as a single large epithelioid cell nodule into which capillaries extend.

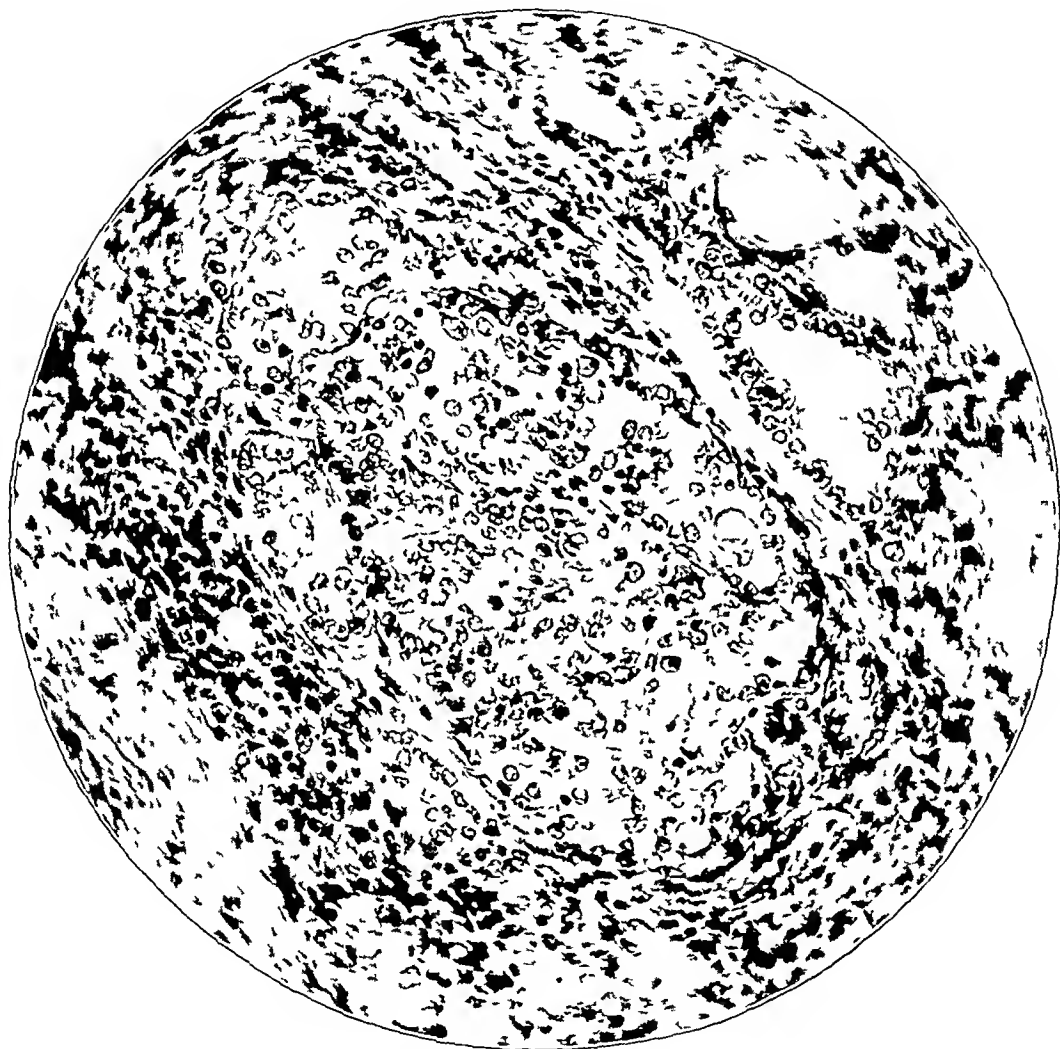


Fig 2 (case 1)—An early stage of the involutional changes which lead to tubercle-like changes. In the left outer portion of the picture is seen the capsule of a node. Closely adjacent to it is a group of small follicles in some of which colloid is still present. There are transitions between the low cuboidal epithelium and larger cells with a distinct cytoplasm and oval nuclei. The follicles are beginning to lose their distinct outlines.

CASE 2—*HISTORY*.—A white woman, aged 37, had thyrotoxic symptoms of moderate severity for over a year. She had lost 25 pounds (11.3 Kg.) during the last six months. The basal metabolic rate was plus 35. She had never been sick before and had two healthy children 7 and 4 years of age. The thyroid was

moderately enlarged and very firm. Partial lobectomy was performed. The portion of gland that was removed weighed 40 Gm and contained many nodules from 5 to 20 mm in diameter. Roentgen examination of the chest was negative.

*Microscopic Examination*—The gland was studded with numerous nodules between which very little unchanged thyroid tissue was left. The nodules were composed of very large, colloid-filled follicles with a low cuboidal epithelial lining. There was a marked epithelial proliferation in the form of cushion-like infoldings lined by cylindric epithelium and made up of very small follicles. Many of the large follicles showed recent or old hemorrhages with iron pigment in the epithelium.

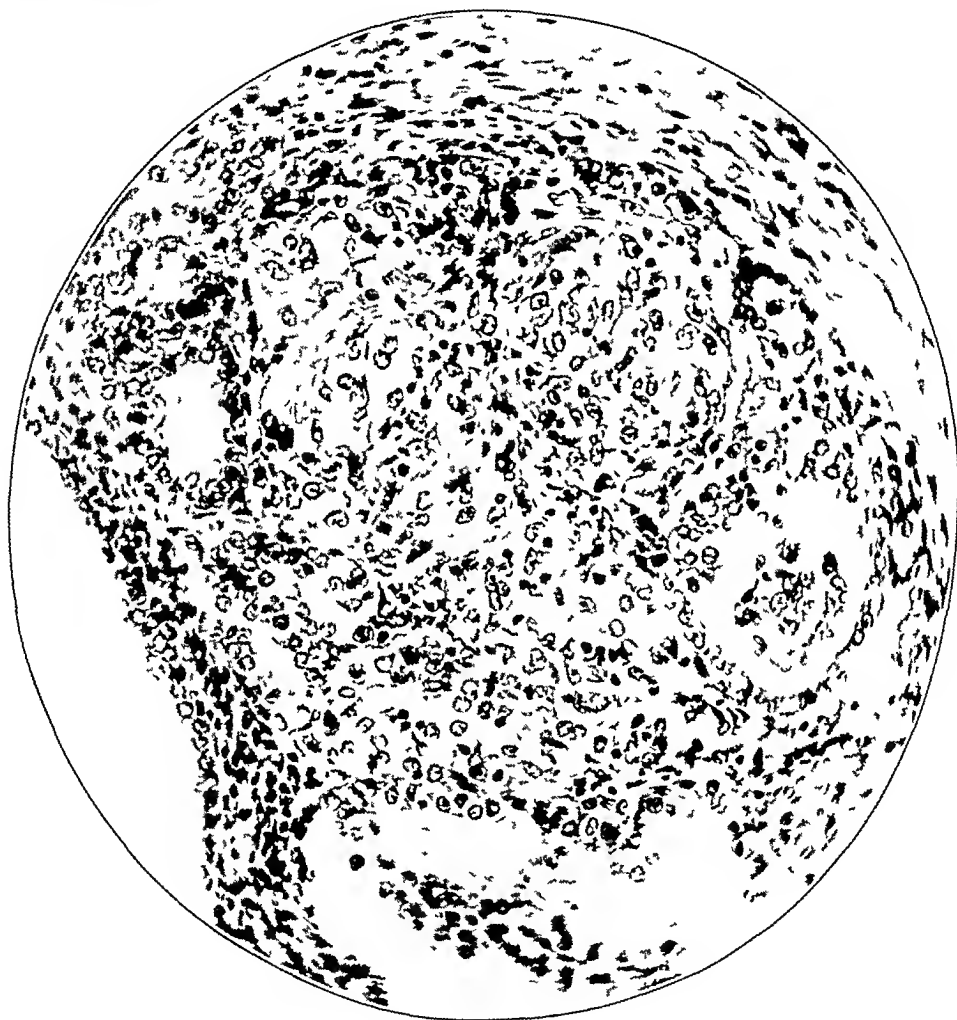


Fig 3 (case 1) —The transformation of the follicle into a tubercle-like nodule has advanced further. Near the center of the field are seen oval cells with an ample cytoplasm. They form a distinct nodule. In the center is a giant cell. In the right lower quadrant, desquamated cells in the lumen of a follicle. They surround a giant cell.

The scanty glandular tissue between the nodules was composed of medium sized colloid-filled follicles. There were many intralobular nodules which consisted of epithelioid cells and giant cells and which were surrounded by a zone of lymphocytes. In the periphery of the nodules were colloid-filled follicles, and one could follow their gradual transformation into the nodules in the same man-

ner as in the first case. Some of the largest nodules measured several millimeters in diameter (fig 4). There was no caseation, and stains for tubercle bacilli did not show any micro-organisms. The changes were restricted to the glandular tissue outside the nodes of thyroid tissue.

CASE 3—*History*—A white woman, aged 25, had had enlargement of the thyroid for six years, and tachycardia at times for one month. There was no tremor, no nervousness, no loss of weight and no cough or expectoration. The family history was negative, and both parents were living and well. Examination

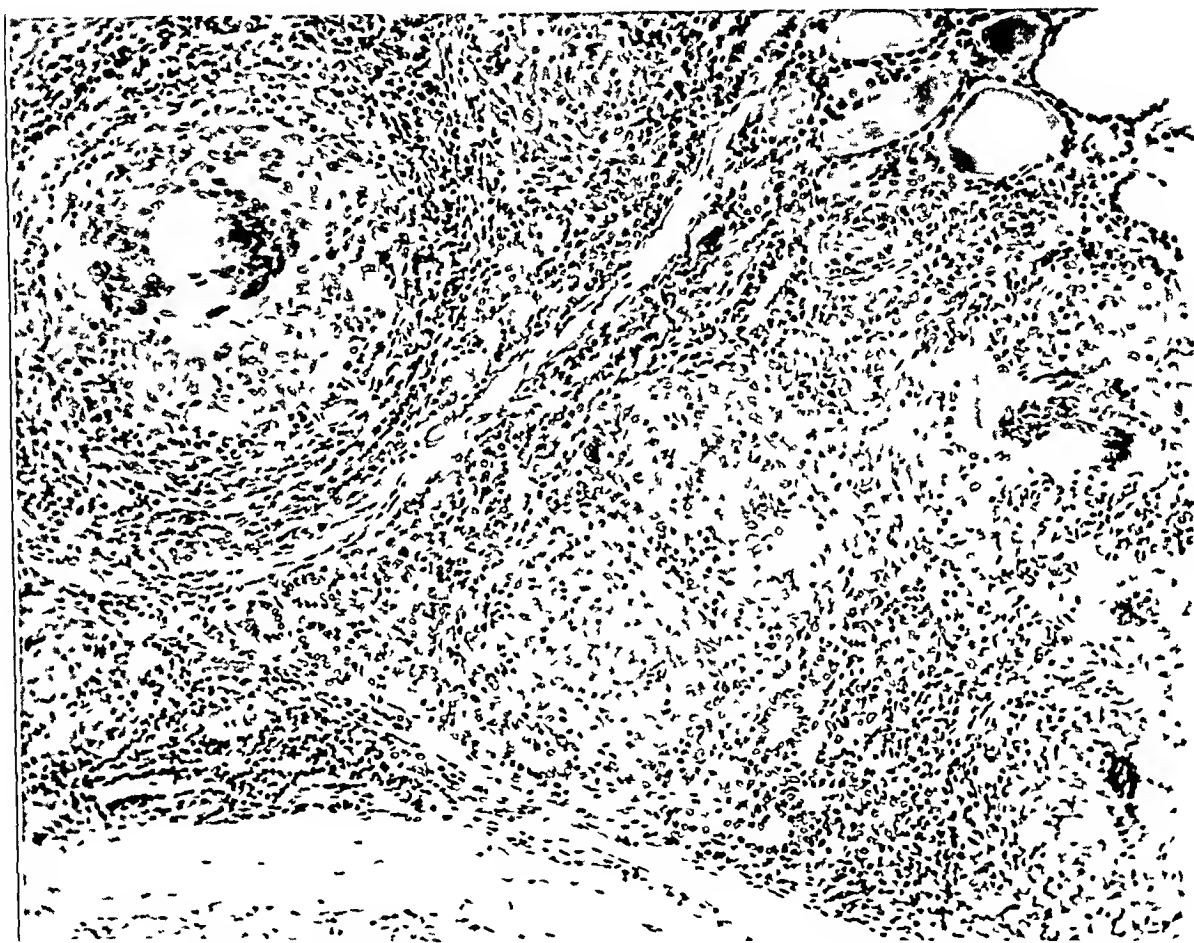


Fig 4 (case 2) —Several nodules of epithelioid cells and numerous giant cells. The nodule in the left upper quadrant still shows its origin from a follicle.

of the chest gave negative results. Both lobes of the thyroid were slightly enlarged. The basal metabolic rate was plus 18. At operation, a small adenoma about 4 cm in diameter was removed with some adjacent thyroid tissue.

*Microscopic Examination*—The node was composed of small follicles which had a low cuboidal lining and were filled with oxyphilic colloid. The follicles were separated by thin strands of fibrillar connective tissue which in places became abundant and hyaline. In the center of the node there were several circumscribed accumulations of pale-stained oval or polyhedral cells. The largest of these accumulations measured about 1 mm in diameter. There were many



multinucleated giant cells. In the center of some of the accumulations there were many slender needles of fatty acid crystals. Some of the light-stained cells contained dark brown pigment granules. The follicles adjacent to these areas showed changes which suggested their gradual transformation into the nodules of epithelioid cells. There was swelling, desquamation and proliferation of the epithelium and the formation of large cells with many nuclei.

**CASE 4—History**—A white man, aged 26, lost 18 pounds (8.2 Kg) in two months. He had had enuresis for two years and nervousness for from three to four years. There was increasing tremor of the hands, and generalized weakness. The appetite was good. The previous history was unimportant, except for tonsillectomy, herniotomy and appendectomy. The patient had had a chronic cough for six months. Roentgen examination of the chest gave negative results. There was marked pulsation of the thyroid, especially of the right lobe. The basal metabolic rate was plus 26, the pulse rate, 108, blood pressure, 146 systolic and 58 diastolic. The portion of the thyroid that was removed weighed 40 Gm. It was uniform and moderately firm.

**Microscopic Examination**—The gland was uniformly composed of medium-sized colloid-filled follicles. Here and there one found a slight hyperplasia of the epithelium and a short papillary infolding. The lobules were separated by a stroma, which did not exceed the normal amount. A few of the lobules contained between their follicles small nodules of epithelioid cells and giant cells surrounded by lymphocytes. The origin of the epithelioid cells and giant cells could be traced to the follicular epithelium, as has been previously described.

#### COMMENT

The histologic changes in the three cases of nodose goiter and in the case of diffuse goiter are identical with those described as a benign, sclerosing form of tuberculosis of the thyroid. There are the circumscribed nodular accumulations of epithelioid cells and giant cells and the peripheral zone of lymphocytes and of dense fibrillar connective tissue. In none of the cases was there any sign of caseation or of other regressive changes. The absence of caseation also is emphasized by Budd and Williams,<sup>11</sup> Smith and Leech,<sup>6</sup> Wegelin<sup>12</sup> and others. In some of their cases Hedinger<sup>9</sup> and Uemura<sup>7</sup> observed caseation which, however, was usually insignificant.

Is the histologic picture in itself a sufficient proof of the tuberculous etiology? This question is justified because, like many other observers (Budd and Williams,<sup>11</sup> Moschowitz,<sup>13</sup> Nather,<sup>14</sup> Arnd,<sup>15</sup> Wegelin<sup>12</sup> and others), I was unable to find acid-fast bacilli. All these observers based their diagnosis on the histologic picture, disregarding the nega-

11 Budd, S. W., and Williams, C. Tuberculosis of the Thyroid Gland, *J. A. M. A.* **92** 1741 (May 25) 1929.

12 Wegelin, C., in Henke and Lubarsch. *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1926, vol. 8, p. 125.

13 Moschowitz, A. *Ann. Surg.* **79** 315, 1924.

14 Nather, K. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **33** 375, 1921.

15 Arnd, C. *Deutsche Ztschr. f. Chir.* **116** 7, 1912.

tive result of the bacterioscopic examination. Very similar cellular reactions, however, occur not only in other infections but also in foreign body granulomas, and if these foreign bodies, cellular or fibrillar débris or inspissated secretions, have disappeared, the differential diagnosis may offer great difficulties. Hence, the demonstration of the bacilli is of paramount importance. A few investigators found the bacilli, e. g., Ruppener<sup>16</sup> in one of three and Smith and Leech in two of three cases. Most successful of all was Hedinger, who detected the micro-organisms in nine of ten cases. He used the antiformin method. I also have tried this method. Blocks of thyroid tissue 2 cm square were cut up on the freezing microtome into sections from 35 to 50 microns thick. The entire group of sections were collected and dissolved with antiformin. After centrifugation the sediment was spread on a large number of slides and stained after Ziehl-Neelsen. The result was negative. As far as the thyroid is concerned, there is one objection to this method. Inspissated colloid, which is rich in lipid material, as shown by its affinity to the lipid stains, may retain the fuchsin almost to the same extent as tubercle bacilli. Débris and small splinters of this acid-fast colloid present in the sediment of the dissolved thyroids can easily be mistaken for tubercle bacilli. Even in sections, the splinters of colloid wedged in between the cells or enclosed in giant cells may resemble acid-fast bacilli.

The negative or doubtful result of the bacterioscopic examination cannot be considered absolute proof against the tuberculous nature of the lesions under discussion. It is well known that in certain forms of tuberculosis the demonstration of the bacilli is exceedingly difficult. In these cases, however, the clinical course, the association with other manifestations of tuberculosis and the result of guinea-pig inoculations confirm the diagnosis. No records on animal inoculations with material from benign tuberculosis of the thyroid are on hand. As mentioned previously, this condition is recognized only under the microscope, and the gross appearance of the gland is little suggestive of it. After the histologic examination is completed, the fresh material usually is no longer available.

In the introduction I have mentioned that autopsy experience and the result of experimental studies suggest a remarkable resistance of the thyroid against tuberculosis. There is the possibility that goitrous changes may increase the susceptibility of the thyroid to tuberculosis. Goiter is not common in tuberculous patients. The thyroid of the people who die from tuberculosis is usually small atrophic and fibrotic. If advanced tuberculosis is associated with a goiter tuberculous changes in the thyroid are not more common than they are in the nonhypertrophic

<sup>16</sup> Ruppener, E. *Frankfurt Ztschr. f. Path.* 2:514, 1909.

gland In only one of eighteen patients who had died from ulcerative pulmonary tuberculosis and whose thyroid contained nodes was I able to find tubercles between the nodes

None of the four patients whose goiter on microscopic examination showed changes suggestive of tuberculosis revealed any other manifestations of this disease The anamnesis and the physical signs were negative, as was the roentgen examination of the chest There was nothing in the clinical picture indicating the peculiar type of goiter The patients showed a mild hyperthyroidism, which was greatly ameliorated by the operation The postoperative course was uneventful, and when later heard from, the patients were in excellent health Similar experiences have been reported by Budd and Williams,<sup>11</sup> Neuhof,<sup>17</sup> Smith and Leech,<sup>6</sup> Crete,<sup>18</sup> Wegelin<sup>12</sup> and, in the majority of their cases, also by Nather,<sup>14</sup> Mosiman<sup>10</sup> and Hedinger.<sup>9</sup> Even if the patients years ago had a cervical lymphadenopathy or a pleuritis or complained of cough or showed other signs of an old and silent tuberculosis this would not necessarily speak in favor of the tuberculous nature of the lesions in the goiter, because both conditions are so common

Many authors emphasize the benign nature of the tuberculosis of the thyroid Nather<sup>14</sup> considered the changes the result of transient invasions of the blood stream by tubercle bacilli without clinical manifestations In order to overcome the negative results of the bacterioscopic examination, some authors resort to the explanation that the nodules in the thyroid are not produced by the tubercle bacilli themselves but by their toxins liberated in some other places of the body From where do the tubercle bacilli and from where do their toxins come, if there is no indication of any other tuberculous lesion in the body? The process in the thyroid is progressing because one can see all the stages of tubercle formation

These considerations induce one to look for another explanation of the tubercle-like structures in goiters There are only two authors to question the tuberculous etiology, namely, Landois<sup>19</sup> and Wilke<sup>20</sup> They expressed the belief that the giant cells are foreign body giant cells about fragments of colloid In Wilke's<sup>20</sup> case there were, however, no epithelioid cell tubercles

The histologic descriptions and the photomicrographs of the cases that I have studied indicate that the epithelioid cells and giant cells are not derived from the histiocytic elements of the stroma but are of epithelial origin The sequel of events is as follows First there is

17 Neuhof, H. *Ann Surg* **79** 313, 1924

18 Crete. *Beitr z klin Chir* **78** 487, 1912

19 Landois. *Arb a d path Inst zu Tuebingen*, 1914, vol 9

20 Wilke. *Virchows Arch f path Anat* **211** 165, 1913

desquamation of the follicular epithelium. The desquamated cells swell up, their cytoplasm becomes slightly oxyphilic and the nuclei assume an oval shape. The free cells resemble epithelioid cells. The number of these cells increases, some fuse together and form multinucleated elements, and finally the cells still attached to the wall undergo similar changes. Thus, the follicle is gradually transformed into a nodule composed of epithelioid cells and giant cells. In the earlier stages there are no reticulin fibers between the cells, an important difference from a mesenchymatous tubercle, which is characterized by an intercellular reticulin net. Later, connective tissue grows in and obscures the histiogenesis. This explanation of the histiogenesis of the tubercle-like nodules in the thyroid has been previously emphasized by Corneli and Ranvier,<sup>21</sup> Baumgarten, Ruppner and others, who believed in their tuberculous nature. In nonspecific chronic inflammations of the thyroid, in particular in Riedel's struma, enormous numbers of epithelial giant cells may be present.

A rudimentary transformation of thyroid follicles into tubercle-like structures in goiters is frequently encountered. Simmonds<sup>22</sup> described such a transformation inside of large lymph follicles which invade the glandular follicles and separate their epithelium into small groups. These changes undoubtedly are involutional. It is this explanation that I advance also for the fully developed nodules, namely, that they are the result of a noninflammatory swelling, degeneration and desquamation of the follicular epithelium that is followed by the ingrowth of fibrillar connective tissue. The fibrous replacement is favored by the fact that the follicles of the thyroid do not possess a membrana propria. What may cause this form of focal involution of newly formed and old follicles is difficult to determine. As mentioned, these changes are much more frequently found in the periphery of and closely adjacent to the nodose hyperplasias than inside the nodes or in the diffuse enlargements. In serial sections of one of my cases I found in the center of some of the tubercle-like nodules clusters of fatty acid needles, which supports the conception of the degenerative nature.

There are no characteristic clinical signs associated with the goiters containing the focal tubercle-like areas of involution, except that the glands are often very firm. The patients may show severe symptoms of exophthalmic goiter or a moderate or slight hyperthyroidism or no toxic symptoms at all (Plummer and Broders<sup>23</sup> Frassi,<sup>24</sup> Mosman<sup>10</sup> Collier

21 Corneli V., and Ranvier, L. *Manual d'histologie pathologique* Paris, 1876

22 Simmonds M. *Virchows Arch f path Anat* **211** 73, 1913

23 Plummer W. A. and Broders A. C. *Minnesota Med* **3** 279 1920

24 Frassi L. *Deutsche Ztschr f Chir* **213** 416, 1929

and Huggins<sup>4</sup> Marcuse<sup>5</sup> Uemura,<sup>7</sup> Neuhoof<sup>17</sup>) A review of the literature shows that the nodules are seven times more common in females than in males. Most of the patients are between 30 and 50 years of age.

I do not deny the existence of a true tuberculosis of the thyroid and of a tuberculous strumitis (Ruppaner<sup>16</sup>). The literature contains reports of a number of well proved cases. There are small or large discrete caseating tubercles or conglomerated tubercles with extensive caseation or cold abscesses. Associated with these changes are tuberculous lesions of the other organs, especially of the lungs, bones or cervical lymph glands. In the literature on tuberculosis of the thyroid these true forms are often grouped together with the tubercle-like changes obscuring the differences between the two conditions (Jones<sup>25</sup> Nathel,<sup>14</sup> Marcuse<sup>5</sup> and others). Before making the diagnosis of tuberculosis of the thyroid one should keep in mind that there occur in goiters tubercle-like structures with extensive fibrosis which are not due to an infection with Koch's bacillus but are the result of focal involutional changes.

#### SUMMARY

In three cases of nodose goiter and in one case of diffuse goiter with mild hyperthyroidism there were found in the removed thyroid tissue nodular structures composed of epithelioid cells and giant cells which resembled miliary tubercles. The origin of these cells could be traced to the follicular epithelium. The patients showed no other signs of tuberculosis and made an excellent recovery. There was no caseation in these nodules, but much fibrosis about them. In spite of a most careful search, tubercle bacilli could not be demonstrated.

The explanation is advanced that the tubercle-like structures are the result of noninfectious focal involutional changes of newly formed and old follicles. These nontuberculous changes should be separated from true tuberculosis of the thyroid.

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25 Jones, T. B. *Am. J. Surg.* 7: 629, 1929.

# POSTOPERATIVE URINARY INCONTINENCE

REVIEW OF LITERATURE AND REPORT OF CASES \*

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BALTIMORE

Loss of voluntary control of the bladder after prostatectomy is very distressing to the patient, as he feels his postoperative plight much more keenly than his preoperative suffering. This is an extreme disappointment to the surgeon as it maims and discounts an otherwise technically perfect operation. The occurrence of incontinence of urine following prostatectomy is more frequent than statistical and general reports would lead one to believe. Fortunately, the mastering and perfection of technic of both the suprapubic and perineal methods of prostatectomy by well trained genito-urinary surgeons has led to a marked disappearance of this very disagreeable and annoying symptom.

The mechanism of urination and the anatomic changes about the neck of the bladder and posterior urethra have been imperfectly understood until recently. During the past fifteen years, genito-urinary surgeons have displayed an increased interest in the ultimate results of prostatectomies, and this has led to numerous investigations into the causative factors of the poor functional results. In this recent period one finds numerous observations recorded about the anatomic and functional condition of the musculature around the neck of the bladder following prostatectomy. Prior to this time, there was a decided paucity of literature dealing with this subject.

## INCIDENCE

Incontinence of urine following prostatectomy has been encountered by practically every genito-urinary surgeon who has performed an extensive series of prostatectomies, irrespective of the method used. The general belief persists, and rightly so, that incontinence occurs more frequently after the perineal than after the suprapubic method. However, in the hands of surgeons specially trained in the perineal technic, the occurrence of incontinence is less than in the hands of untrained surgeons.

According to the statistical studies of various surgeons postoperative urinary incontinence is a relatively infrequent condition. However, we

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Submitted for publication Dec 21, 1929

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feel that if accurate follow-up investigations were made in cases of prostatectomy, a greater percentage of urinary incontinence, either complete or partial, would be found to exist. The vagueness of the term incontinence may account for the variability of the results reported.

The necessity for a definite terminology in regard to incontinence is evident. The term true or complete incontinence implies the complete loss of control of urination and the existence of urinary dribbling at all times. The term, partial or incomplete incontinence, implies a partial or faulty control of urination with the occurrence of dribbling between urination on exertion or at the end of urination, other than the amount of leakage one ordinarily sees in a normal person when the anterior urethra is not stripped.

The degree of incontinence may vary in the same or different persons. It may be temporary or permanent and hence of slight or serious importance.

Temporary incontinence, lasting several days or weeks, is a rather frequent occurrence after a suprapubic or perineal prostatectomy, but more so after the latter method. Fortunately, the condition responds to treatment very well. The cause of such incontinence may be a slight cicatricial contraction in the prostatic urethra or about the vesical neck, and instrumental dilation at frequent intervals results in complete restoration of function. Occasionally, a temporary incontinence is associated with an anesthesia of the urethra and vesical neck which is the result of trauma incidental to the removal of the prostate. These patients are not conscious of urine passing through the urethra. If the nerve supply is intact, the sensation of urination is soon restored and control of urination reestablished.

Some patients have a slight incontinence when standing or walking for the first time. Some do not dribble when resting or reclining but on assuming an upright position, such as standing or walking, they dribble a few drops. The latter two forms of incontinence disappear rapidly as the patient gains control of urination. In the first few days of convalescence when urine is voided through the urethra, the patient should be instructed how to start and stop his stream voluntarily several times during each act of urination and to void at frequent intervals in order to improve the tone of the vesical sphincters and to facilitate control of urination. The importance of these bladder exercises has been stressed by Alexander.

Often in old and debilitated patients there may develop a terminal dribbling accompanied by a marked frequency and urgency. If this condition should persist, it may result in a true complete incontinence as the sphincteric control is gradually lost. Permanent incontinence is associated with some anatomic or mechanical defect involving both sphincters and is the result of operative manipulation.

Incontinence may also be diurnal or nocturnal or both. Diurnal incontinence is usually partial and temporary, and manifests itself when the patient is up and about on his feet in the first few days of voiding. It responds well to therapy, such as dilatations of the posterior urethra, and disappears in a very short time. Nocturnal incontinence seldom occurs alone but is usually accompanied by diurnal incontinence, and these combined must be considered as a true or complete incontinence which is of grave prognostic significance.

Series of different types of prostatectomies have been reported by many authors with some reference to incontinence. In 1902, Parker Syme reported three cases of incontinence following thirteen perineal prostatectomies. In 1904, Watson made a very complete resume of the results and complications in an extensive series of prostatectomies. He noted the occurrence of incontinence of urine in 3.5 per cent of a series of 530 perineal prostatectomies and 2.6 per cent of 1,086 cases in which Bottini's operation was done. He made no mention of urinary incontinence in the series of 243 suprapubic prostatectomies. Escat (1904) reported 12 cases (3 per cent) of urinary incontinence in 382 cases of perineal prostatectomies. Ruggles reported 5 cases (13 per cent) of incontinence in 39 prostatectomies, presumably of the perineal type. Pauchet reviewed a series of 50 perineal and 152 suprapubic prostatectomies but did not find any definite cases of incontinence. However, he stated that certain patients lost a little of their urine. This complication lasted several weeks or months but always disappeared. The patients who presented the symptoms of incontinence for the longest time had some affliction of the nervous system.

Ertzbischoff (1911) studied the late complications of transvesical (suprapubic) prostatectomies and found 11 cases in 1,573 operations. In most cases, the cause was a lesion of the membranous urethra which normally should be avoided. In 1912, Fieyer reviewed a series of 1,000 suprapubic prostatectomies and did not mention a single case of incontinence except to state that in 1 case the patient failed to regain the power of voluntary micturition. He attributed this to a flaccid bladder paralyzed by the extreme overdistention present before the catheter was employed to relieve the condition.

In 1911, Judd reviewed a series of 532 cases, which included 323 perineal and 140 suprapubic prostatectomies for benign hypertrophy of the prostate and 50 perineal and 19 suprapubic prostatectomies for carcinoma of the prostate. He stated that urinary incontinence following prostatectomy is a rare occurrence. He did not have a case of incontinence following suprapubic prostatectomy for benign hypertrophy although 2 patients, operated on by the suprapubic route who did not have complete control before operation, were not relieved. In 2 patients who had suprapubic operations for carcinoma, good control



of urination was present for some time after the operation but incontinence gradually developed on recurrence of the old trouble. He stated that there were 7 cases of perineal prostatectomy with some degree of incontinence, in some of which there had been dribbling before operation. In 3 of these cases there was a history of an old syphilitic infection, but there was no evidence of syphilis at the time of operation. In addition to the aforementioned cases, there were 11 patients on whom perineal prostatectomy had been performed whose retentive power was not strong but who could hold their urine several hours before dribbling. Several patients did not have good control immediately following operation but regained it in several weeks. Some had difficulty in retaining urine when in the recumbent position. Others had good control while lying down but leaked a few drops when they were in the upright position.

Gardner, in his large series of cases, had never seen incontinence following a perineal or suprapubic prostatectomy, and he attributed this to the preservation of the compressor urethrae muscle. In a series of 450 perineal prostatectomies reported by Young, in 1911, complete incontinence—dribbling day and night—did not occur in a single instance, and only three cases of partial incontinence occurred. In the second volume (page 461) of his "Practice of Urology" he has tabulated the results of 55 cases of suprapubic prostatectomy and reported incontinence in 3 cases (5 per cent).

In Deaver's collected series of 1,734 suprapubic cases and 676 perineal cases, this complication occurred 46 times (2.6 per cent) in the suprapubic series and 36 times (5.1 per cent) in the perineal series. Forty-one of these 46 cases of incontinence following suprapubic prostatectomy are reported by one correspondent as occurring among 75 patients. McDonald mentioned 3 cases of incontinence in his analysis of the suprapubic cases in which operation was performed at St. Peter's Hospital, London.

Martin, in an analysis of the results in a series of 110 patients on whom prostatectomy was performed (55 cases each of the perineal and suprapubic method) gave definite information concerning incontinence in 50 perineal and in 46 suprapubic cases. In the perineal series 32 patients (64 per cent) had full control of the bladder, 11 (22 per cent) partial incontinence and 7 (14 per cent) complete incontinence. In the suprapubic series 37 (80.5 per cent) had full control, 7 (15.2 per cent) had partial control of the bladder and 2 (4.3 per cent) complete incontinence.

Hinman recorded observations based on 90 perineal and 38 suprapubic cases. He mentioned dribbling in 1 perineal case complicated by cerebral syphilis. Dribbling at the end of urination was present in 37 per cent of the suprapubic and 20 per cent of the perineal cases.

Dribbling on exertion between urination existed in 26 per cent of the suprapubic and 9 per cent of the perineal cases

Swan reviewed the functional results of a series of 100 cases of all types of operations on the prostate and noted a restoration of urinary control to normal in 82 per cent. Analysis of his results reveals that leakage, or dribbling of urine, occurred in 7 of the 54 cases of one-stage suprapubic prostatectomy, in 1 of the 23 cases of two-stage suprapubic prostatectomy, in 5 of the 9 cases of perineal prostatectomy and in 5 of the 14 cases of punch prostatectomy

E. Davis reported the late results of perineal prostatectomy ascertained by questioning 100 consecutive patients in a series of 176 cases. There was no case of complete incontinence, 2 patients had a sufficient degree of incontinence to cause considerable inconvenience and 2 others had a slight degree of incontinence. In the former (2 cases with inconvenient incontinence), each of the patients had intervals of complete dryness and the ability to start and stop the stream at will several times while voiding. However, there was a weakness of the external sphincter as indicated by leakage of small amounts of urine following undue exertion such as coughing, sneezing and sudden rising.

Cecil reported one case of incontinence in 234 consecutive prostatectomies. His series includes 201 cases of perineal prostatectomy for benign hypertrophy of the prostate, 15 cases of suprapubic prostatectomy for benign hypertrophy of the prostate and 2 cases of suprapubic prostatectomy for carcinoma of the prostate. He does not state the type of operation following which the incontinence occurred.

The figures of Whiteside based on 1,423 cases in which prostatectomy was performed by suprapubic and perineal routes are of interest. He reported 24 cases of urinary incontinence all of which followed perineal prostatectomies.

We have recently reviewed a series of 220 prostatectomies performed by us and noted the occurrence of incontinence of urine in 1 case (0.7 per cent) in 134 suprapubic prostatectomies and in 5 cases (5.8 per cent) in 86 perineal prostatectomies. The suprapubic case was one of partial incontinence. Of the 5 perineal cases, there was complete incontinence in 2 and partial incontinence in 3.

Here and there in the literature one finds isolated reports of a case of incontinence following prostatectomy associated with some abnormal change in the musculature about the vesical neck. Fullerton reported 3 cases of stenosis of the internal orifice of the bladder after suprapubic prostatectomy, and in 2 there was incontinence.

#### ANATOMY

Before a discussion of the nature of the changes in the musculature about the vesical neck and the posterior urethra following operative

intervention is undertaken, a brief description of the normal anatomic relations of these structures will aid in understanding the postoperative and pathologic observations

Anatomists differ greatly on the exact muscular components of the sphincters of the bladder. The most accurate work in this field was performed by Wesson in 1920 and by Young and Wesson in 1921 in a comprehensive and excellent anatomic, embryologic and surgical study of the trigone of the bladder. In the following descriptions, we have drawn very largely from their studies and observations.

*The Bladder*—The bladder has four coats, but for the greater part is made up of two ill defined layers of smooth involuntary muscle—an external longitudinal and an internal circular layer. The arrangement and direction of these layers are difficult to ascertain, for they change and rearrange themselves with each change in the size of the bladder. It has been agreed that the entire musculature of the bladder contracts together and thus acts as one muscle, which is called by some writers, the “detrusor of the bladder.”

*The Trigone*—At the base of the bladder there is a distinctly separate layer of muscle superimposed on these two layers of bladder muscle which is known as the trigonal muscle. This muscle is of mesodermal origin while the two layers of bladder muscles are of endodermal origin. The trigonal muscle is in reality an extension of the longitudinal muscle layers of the ureters and their sheaths. The fibers that compose this muscle spread out in a fanlike direction from each ureteral orifice. Some of these fibers spread medially from each ureteral orifice, meeting and forming Meier's intra-ureteric bar. Some fibers interlace in the middle of the trigone with the corresponding fibers of the other side and still others pass downward into the urethra to form the muscles of Bell. The muscles of Bell on each side apparently converge at the vesical neck to form a thickened layer of muscle passing over the posterior edge of the vesical orifice known as the uvula of Lieutaud.

The mucous membrane of the trigone differs markedly from that of the remainder of the bladder in that in the former instance it is far more intimately adherent to the subjacent tissues and does not present any rugae when the bladder is empty, thus preventing any prolapse of the mucous membrane into the vesical orifice during micturition.

*The Internal Vesical Sphincter*—The internal vesical sphincter is made up of muscle fibers from the external longitudinal and internal circular layers of the bladder musculature. Most of the fibers from the external longitudinal layer on the posterior surface of the bladder pass downward to end abruptly in the region of the vesical neck. Other fibers from this layer pass along the posterior surface of the bladder to the vesical neck where they diverge slightly and pass downward and

forward on either side in the form of muscular bands. These bands swing medially to form a continuous loop or arch about the urethra at its very upper limit just beyond the prostate. This muscular loop is known as the external arcuate muscle of the vesical orifice. The fibers from the internal circular layer of the bladder pass around the bladder neck down to the vesical orifice at which point it becomes a thin band lying inside the loop formed by the fibers from the external longitudinal layer (as previously described). The inner thin loop is known as the internal arcuate muscle of the vesical orifice. The formation of this muscle is dependent on some of the fibers of the internal circular layer on the posterior surface of the bladder passing downward and forward in an oblique direction in the form of a loop or arch in front of the urethra in the region opposite the verumontanum (fig 1).

There are elastic tissue fibers interspersed among these smooth muscle bands at the vesical orifice, and, in addition, some of these

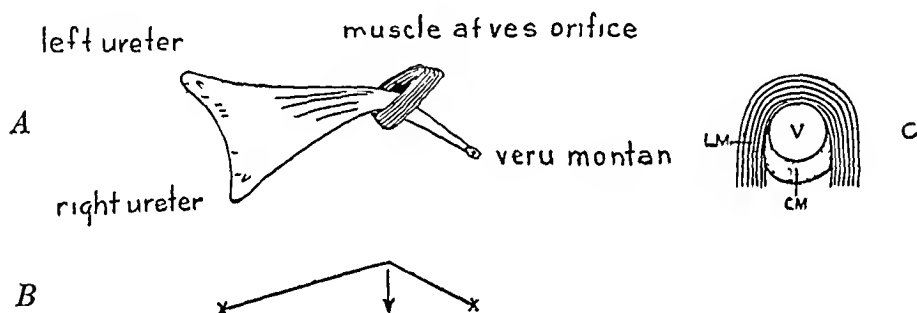


Fig 1—Diagrams to show the effect of contraction of the trigone in opening the internal vesical sphincter. *A* indicates the trigonal muscles passing through the lateral muscles of the sphincter and over the uvula vesicae, *B*, the effect of contraction of the arc-shaped trigonal muscle, viz, to pull down the uvula vesicae and open the sphincter, *C*, cross-section of the vesical orifice (*V*) showing the upward pull of the loop from the circular muscle (*CM*) and the opposing action of the longitudinal muscle (*LM*) loop (After Young Practice of Urology, vol 1, figs 3 and 5)

elastic fibers from the external longitudinal layer of the bladder pass downward to form an interlacing network between the deeper layers about the vesical orifice.

The internal vesical sphincter is thus composed of two loops of smooth muscle: the external arcuate muscle of the vesical orifice derived from the external longitudinal layer of the bladder and the internal arcuate muscle of the vesical orifice derived from the internal circular layer of the bladder. The internal sphincter is in reality a surgical designation and not an anatomic entity, since it is not a simple circular sphincter, like the sphincter ani, with an origin and an insertion in itself. Its function will be discussed later.

*The External Sphincter of the Bladder*—The external sphincter is situated at the level of the triangular ligament and is composed of striated voluntary muscle. It is innervated by the internal pudic nerve. This sphincter has its origin in a group of striated muscle fibers that are slightly anterior to the external arcuate muscle of the vesical orifice at its mediolateral aspect. These fibers pass in a circular direction in relation to the urethra and at first do not surround the urethra entirely. As they pass downward and forward to the apex of the prostate, they increase in number and completely surround the urethra, and at the level of the triangular ligament they form a thick circular band with a raphe due to the interlacing of fibers from each side.

*The Compressor Urethrae*—The compressor urethrae is composed of striated voluntary muscle fibers which covered the entire membranous urethra. It has the same origin as the external sphincter and is essentially the striated muscle fibers that are first posterior to and lead up to the external sphincter. In the literature there is a decided tendency to an interchangeability of the terms, compressor urethrae and external sphincter, and very often both are included under the name of either muscle. This may be easily understood when one realizes that both muscles have the same origin and innervation and essentially the same function.

*Intrinsic Smooth Musculature of Posterior Urethra*—In addition to these striated muscle fibers, the urethra has a well defined internal longitudinal and poorly defined circular layer of smooth involuntary muscle which are derived from the muscle layers of the bladder and trigone. The inner longitudinal layer of smooth muscle on the anterior aspect of the posterior urethra is derived from the external longitudinal layer of the bladder, and on the posterior aspect from the trigonal muscle as it passes down over the posterior margin of the vesical orifice. The internal longitudinal muscle fibers extend down to the membranous urethra ending in the region of Cowper's glands. There are also a few circular smooth muscle fibers surrounding the urethra in the region of the vesical sphincter which are derived from the muscular components of the arcuate muscles at the vesical orifice. The prostatic urethra for a short distance extending from the vesical orifice to a point about half way down to the verumontanum is devoid of fibers derived from the internal circular layer of the bladder. However, Young and Wesson have pointed out that the fibers from this layer extend into the prostate gland where their course cannot be traced and it is very likely that these circular fibers have been invaded and distorted by prostatic tubules and that the composite mass represents the prostate gland.

The two layers of intrinsic smooth muscle in the posterior urethra together with the internal vesical sphincter are innervated by symp-

thetic fibers from the inferior mesenteric and from prostatic and cavernous plexuses through the hypogastric plexus

#### THE MECHANISM OF URINATION

The correlation of physiologic and neuro-anatomic studies with cystoscopic and surgical observations has served to clarify the complex mechanism of urination. In this respect the observations and studies of Young and Wesson, Graves and Davidoff, Rose and Deakin, Elliot and McClintic are of great value. The nervous and musculature mechanisms involved in the act of urination are rather complicated and recently have been the subject of comprehensive study. While complete infor-

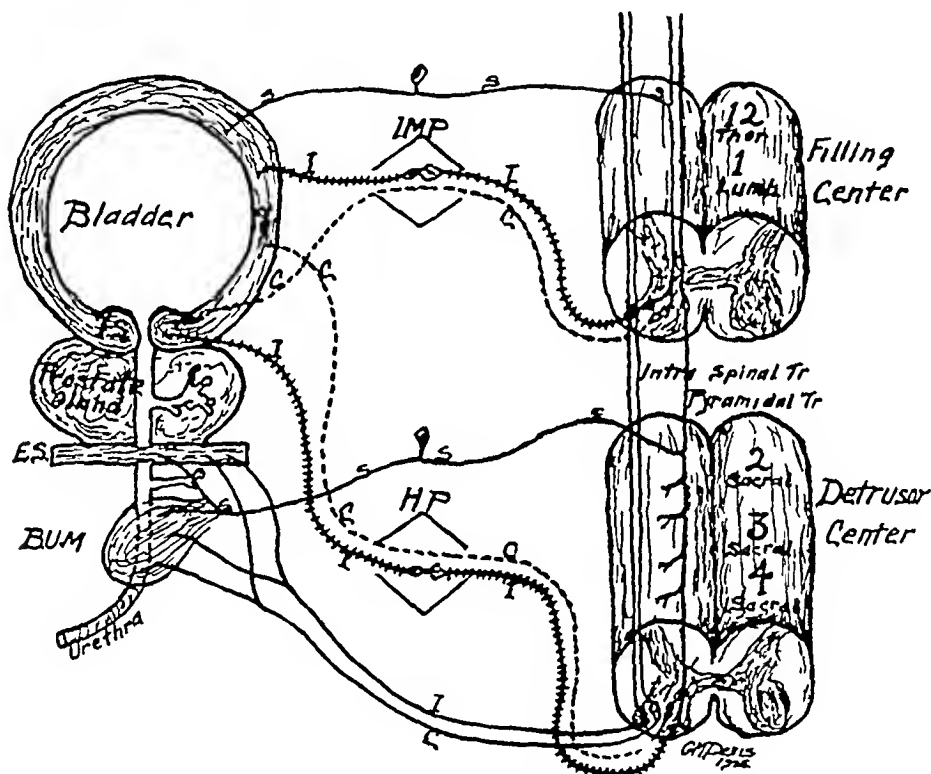


Fig 2—Detrusor mechanism (nerve supply). *H P* indicates the hypogastric plexus, *IMP* inferior mesenteric plexus. The nerve fibers are indicated as *I*, inhibitor, *C*, contractor, *IS*, internal sphincter, *ES*, external sphincter, *BUM*, bulbo-urethral muscle, and *S*, the sensory muscle. (After McClintic, *J Urol* 20:269 [Sept] 1928.)

mation is still lacking, several facts have been clearly established in regard to urination. In the following discussion it is our intention to present a brief review of the accepted facts and theories concerning urination.

*Nerve Supply of the Bladder (fig 2)*—Studies reveal that the bladder has a bilateral nerve supply as each half of the bladder has its own innervation. The trigone has a richer nerve supply than the

remainder of the bladder. The main nerve trunks enter the bladder in the region of the ureters after passing through the peripheral ganglions found about the base of the bladder. There are two sets of nerves supplying each half of the bladder.

1. The parasympathetic nerves, known as the pelvic splanchnic nerves or *nervi erigentes*, are made of fine medullated fibers which are derived from the anterior branches of the sacral plexus at the level of the second, third and possibly the fourth sacral nerves. These nerves pass to the pelvic or hypogastric plexus at the base of the bladder.

2. The sympathetic nerves (hypogastric nerves) are of the non-medullated type and arise from the white rami communicantes of the lumbar nerves. They pass through the aortic plexus to reach the inferior mesenteric ganglion. From this ganglion, two main nerve trunks (hypogastric nerves) pass down along the sides of the rectum, one on each side, to the pelvic plexus.

In the pelvic plexus, one finds that the spinal fibers unite with the sympathetic fibers, and the nerves from the pelvic plexus to the bladder are mainly nonmedullated fibers. Three ganglions of the pelvic plexus are especially concerned in the innervation of the bladder.

(a) The superior (or rectovesical) ganglion, which lies in front of the rectum and sends a few fibers to the superior surface of the bladder.

(b) The major vesicoseminal ganglion, which lies on the base of the bladder and supplies the superior, lateral and anterior bladder surfaces.

(c) The minor vesicoseminal ganglion, which lies on the base of the bladder but more mesial than the previous ganglion and sends fibers to the base of the bladder and to the ureters.

On reaching the bladder wall, all the nerves divide into many fine branches which are distributed to the various layers of the bladder. The nerves transmitting sensory impulses are found in all four layers of the bladder. The motor nerves relay in the ganglions and plexuses of the outer layer of the bladder and from here send fibers to the musculature of the bladder. In the submucosa are found several minute ganglions from which filaments arise and penetrate the mucosa to end between the epithelial cells. The inhibitory fibers terminate in the muscular coat.

The afferent bladder impulses reach the spinal cord through sensory nerves. The majority of the afferent impulses pass through the pelvic splanchnics (*nervi erigentes*) to reach the cord by way of the posterior roots of the second, third and possibly the fourth sacral nerves. A small number of these impulses are thought by some observers to pass through sensory filaments in the hypogastric plexus to reach the cord by way of the twelfth thoracic and the first and second lumbar nerves.

These sensory neurons end (*a*) in the second, third and fourth sacral segments of the cord, and (*b*) in the twelfth thoracic and first and second lumbar segments of the cord. They make connections with the motor neurones in the ventral horn cells of the cord directly as a reflex arc or by association paths as a part of a reflex system. Thus, when the posterior roots of the nerves supplying these spinal segments are stimulated, the motor fibers to the bladder in the anterior roots of the nerves are reflexly excited.

The association tracts connecting the thoracolumbar and sacral parts of the cord are the intraspinal tracts found in a solitary spinal fasciculus. The latter tract is an association path which connects not only the visceral centers of the different levels of the spinal cord but also those of the medulla oblongata, forming a continuous visceral mechanism. As McClintic points out, the mechanism so formed is protective and automatic and represents the mechanism of instincts also described as the primitive reflexes or the mass reflex system.

The efferent or motor paths from the cord to the bladder are also confined to the parasympathetic system (*nervi erigentes*) and the sympathetic system (hypogastric nerves). Their various pathways through the intrinsic and extrinsic ganglions and their excitator and inhibitory elements are considered later in relation to the emptying and filling mechanisms of the bladder.

In view of the foregoing observations, we can say with some degree of certainty that the spinal cord center for micturition is found in the lower part of the cord (lumbosacral region) and is more or less localized to separate segmental areas: (*a*) the center for "the bladder-filling mechanism," localized in the twelfth thoracic and first lumbar segments and controlling the sphincter area, (*b*) the center for the emptying mechanism of the bladder, localized to the second, third and fourth sacral segments and controlling the detrusor muscle. Halliburton (quoted by Graves) considered the sacral segment of the cord as the spinal center for micturition, for he maintained that the micturition reflex remains intact in animals whose cord is cut across in the lower lumbar region. Starling (quoted by Graves) expressed the belief that the lumbosacral region serves as the spinal center, since micturition is possible when the thoracic portion of the cord is severed and the reflex arcs of the lower cord are left intact.

The cerebral centers for urination are less clearly defined. Kletschmer quoted Czyhlarz and Marbury as claiming the existence of three such cerebral centers: a center in the cortex of the motor area where the arm center goes over into the leg center, a center in the corpus striatum and a center in the optic thalamus. Tigerstedt (quoted by Graves) suggested a center in the anterior part of the sigmoidal gyrus since stimulation of this area in a cat produces contraction of the bladder.



with the impulses passing through the thalamus, clura, cerebellum and medulla to the cord. The spinal path for motor impulses from the brain to the bladder is generally conceded to be in the posterior part of the pyramidal tract of the lateral column.

*Neuromuscular Mechanism (Fig 2)*—The bladder, like the anus and the uterus, has a combined voluntary and involuntary mechanism. In the bladder, this mechanism is called the detrusor mechanism and is made up of a filling and emptying system. Both the filling and emptying mechanisms consist of an inhibiting (relaxing) and an excitator (contracting) element which are correlated. The bladder, like other viscera, has a double innervation wherein impulses transmitted through a parasympathetic system are antagonistic to those transmitted through a sympathetic system.

The filling mechanism is entirely involuntary (automatic or autonomic). The center for this mechanism is located in the twelfth thoracic and first lumbar segments of the spinal cord. The "nerves of filling the bladder" are sympathetic in character and are called the hypogastric nerves which are derived from anterior roots of the spinal nerves from the aforementioned spinal segments. These nerves pass through the inferior mesenteric ganglion and plexus to supply the bladder and internal sphincter. The inhibitory fibers relay in the peripheral ganglion (inferior mesenteric ganglion) to end in the muscular layer of the bladder. The excitator (contracting) fibers relay in the intrinsic (bladder) ganglion and supply the internal vesical sphincter. Stimulation of the "nerve of filling" produces a relaxation of the bladder wall (detrusor) and a contraction of the internal vesical sphincter.

The emptying mechanism is partly involuntary and partly voluntary. The involuntary part differs from the filling mechanism in that the center for the emptying mechanism is in the second, third and fourth sacral segments of the spinal cord, and the peripheral ganglions and plexuses are in the pelvic (hypogastric) plexus. The emptying and filling centers are connected by means of an association pathway (solitary spinal fasciculus) or an intraspinal tract of association fibers. The nerves of emptying concerned in the involuntary system are parasympathetic in character and are called the nervi erigentes (pelvic splanchnics). Inhibitory fibers of these nerves pass to the internal vesical sphincter after relaying in the peripheral ganglion (hypogastric plexus). The excitator fibers relay in the intrinsic ganglions of the bladder walls to end in the muscular coat of the bladder. Stimulation of these parasympathetic nerves of emptying causes a contraction of the bladder (detrusor) and a relaxation of the internal vesical sphincter.

The voluntary part of the emptying mechanism involves two striated muscles: external vesical sphincter (compressor urethrae) and the bulbo-urethralis (accelerator urinae) muscles which are supplied by

the perineal branch of the internal pudic nerve, a spinal nerve. The voluntary system also has its center in the second, third and fourth segments of the spinal cord. The peripheral afferent or sensory path of the involuntary system is essentially the same, physiologically as the involuntary system of the emptying mechanisms, for the sensory neurons from these areas make the same local connections in the second, third and fourth sacral segments, but in addition it makes connections with the sensory areas of the cerebrum.

The efferent or motor path of the voluntary system, however differs, as in the former instance the motor neurons pass directly to the muscles without relaying in the extrinsic ganglions or ending about intrinsic ones. The excitator and inhibitory impulses to these muscles originate in the cerebrum and the spinal cord centers by way of the pyramidal tracts. The cerebral center for inhibition of the voluntary part of emptying mechanism is presumably in the frontal area. The inhibitory impulses transmitted through the pyramidal tract serve a double purpose. (a) They permit the voluntary muscle to relax while their functional antagonists contract and (b) they inhibit reflexes. It is thought by some observers that the sensation of pain in the region of the bladder is transmitted through the pudic nerve. Stimulation of this nerve causes a contraction of the posterior urethra which is of short duration.

In other words, the detrusor mechanism is a diphasic mechanism and consists of two parts, a filling and an emptying system. The filling of the bladder is an involuntary phenomenon which requires a relaxation of the musculature to permit distention and a contraction of the interior vesical sphincter to keep the bladder closed. When the bladder is distended, the internal involuntary sphincter relaxes as a result of reflex stimulation of the spinal centers by afferent bladder impulses, and unless urination takes place further closure must be maintained by the external voluntary sphincter. The emptying of the bladder is in part involuntary and in part voluntary. The involuntary system requires a contraction of the bladder musculature and a relaxation of the internal vesical sphincter which is combined with a relaxation of the external vesical sphincter.

*The Muscular Mechanism of Urination (Figs 3 and 4)*—The muscular mechanism in the act of urination functions in an orderly manner. In the normal male, micturition is voluntarily initiated. In the first motion there is a voluntary depression of the internal sphincter and prostatic urethra by the levator prostatae (a portion of the levator ani muscle) and to a less extent by the recto-urethralis muscle. This results in a downward depression of the internal orifice and a straightening out of the curve of the prostatic urethra to overcome the resistant angle of the membranous urethra which is depressed by the deep trans-

verse perineal muscles. The actual emptying of the bladder is the result of an involuntary mechanism which requires an inhibition (relaxation) of the internal sphincter and a simultaneous contraction of the whole bladder musculature (detrusor). This latter mechanism is dependent on afferent stimuli caused by the distention of the bladder reaching the spinal cord centers through the sympathetic system, and here, through intersegmental (reflex) connection, efferent impulses arise which cause the trigonal muscles to contract. The contraction of the trigonal muscles results in the opening of the internal sphincter and foreshortening the posterior urethra above the verumontanum. The contraction of

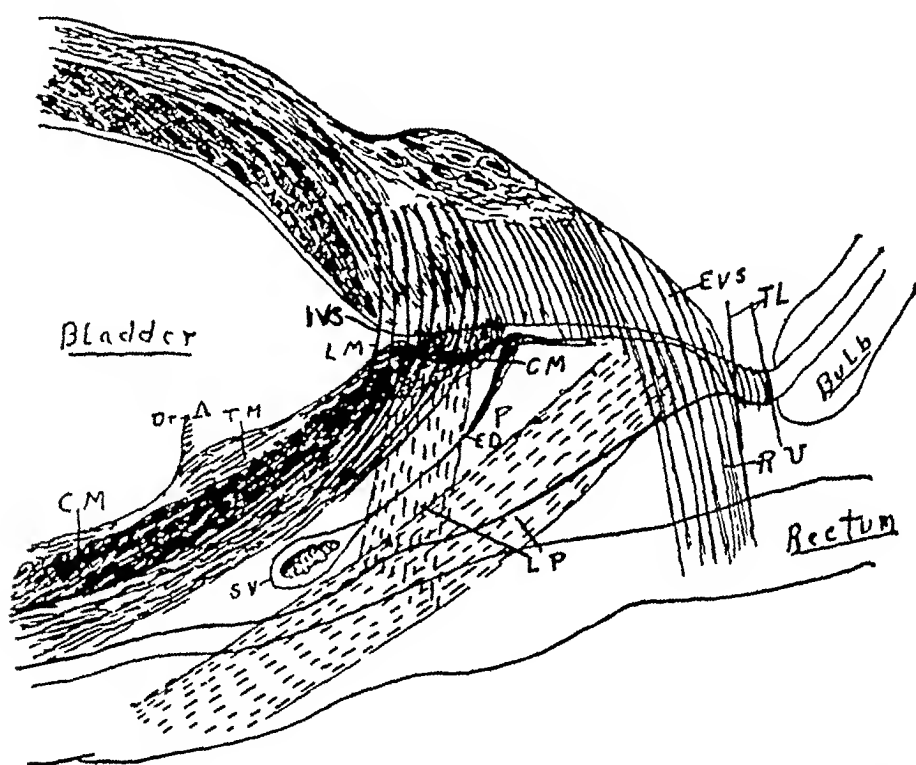


Fig 3—Micturition, sphincter closed. Note the angularity existing between the pendulous urethra (at bulb) and the prostatic urethra. RU indicates the recto-urethralis muscle, LP, the levator prostatae (striated) muscle (part of the levator ani muscle), EVS, the external vesical sphincter (striated), IVS, the internal vesical sphincter (nonstriated), with LM, longitudinal muscle, and CM, circular muscle, TM, the trigonal muscle, P, the prostate, ED, the ejaculatory duct, SV, the seminal vesicles, U, the ureter, TL, the triangular ligament (two layers), Bladder LM, the longitudinal muscle, and Bladder CM, the circular muscle. (After Redewill J A M A 91 1960 [Dec 22] 1928.)

the trigonal muscles is associated with or institutes the contraction of the bladder wall (by the action of the parasympathetic nerves). The external sphincter which is under voluntary control then relaxes, and the bladder is emptied. During urination, the striated muscles about the posterior urethra (compressor urethrae, bulbocavernosus and trans-

verse perineal muscles) are in a state of relaxation, for by a voluntary contraction of these muscles the stream can be cut off at will. When the bladder is emptied, the internal sphincter closes and the last portion of urine escaping from the bladder into the urethra in the male is ejected in spurts due to the rhythmic contractions of the compressor urethrae and the bulbocavernosus muscle. Following this, there is a relaxation of the entire voluntary musculature including the external vesical sphincter. The bladder now returns to a state which will permit filling and distention.

Young was the first to emphasize the rôle of the trigone in the mechanism of urination. His original observations on the action of

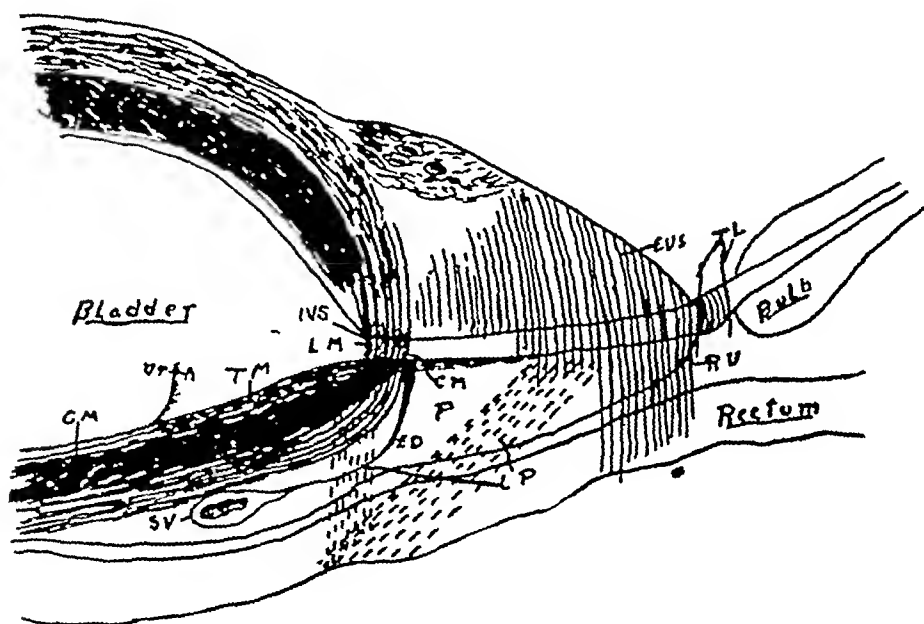


Fig 4—Micturition, sphincter open. The nomenclature is the same as in figure 3. Note the angularity of the prostatic urethra reduced with the sphincter relaxed, the urethra becoming almost a straight tube during micturition. (After Redewill J A M A 91 1960 [Dec 22] 1928)

the trigonal muscle were made on a patient who had a violent desire to void during a cystoscopic examination. He observed a violent contraction of the trigone and Bell's muscles and a thickening and shortening of the ureteral ridges and Mercier's intra-ureteric bar. He noted that the posterior lip of the vesical orifice flattened out and disappeared due to the contraction of the trigonal muscle which, as has been described before, passes downward over the posterior margin of the vesical orifice into the posterior urethra in the form of an arc. By its contraction, the trigonal muscle pulls down on the internal vesical orifice and opens the sphincter, forming a triangular wide open hole through which the urine may escape. Its contraction also causes a

shortening of the posterior urethra thereby pulling the verumontanum up almost into the bladder. These observations were confirmed by Young and Wesson in their extensive study of the trigone.

*Micturition Reflexes*—It is of historical interest to recall the theory of the mechanism of urination advanced by Goetz in 1874. He maintained that distention of the bladder eventually produces a reflex contraction of the bladder walls which squeezes a few drops of urine into the posterior urethra and that the desire to void arose from a stimulation of the sensory nerves of the posterior urethra. This view found support in the fact that stimulation of the posterior urethra by instruments, chemicals or inflammatory reactions causes a desire to void.

The fallacy of this theory is evident when one considers that women have no prostatic urethra and that in many males the prostatic urethra fails to respond to any stimulation. Walker has also pointed out that in cases in which the entire prostatic urethra was removed during a suprapubic prostatectomy there was no appreciable difference in the sensation to void. He also pointed out that in many cases of suprapubic prostatectomy the prostatic urethra became a part of the bladder and naturally held some urine, yet the desire to void came only when the bladder was distended.

In 1882, Mosso and Pellancani studied the volume of the bladder in women with the aid of a catheter, and were the first to show that the desire to void arose from stimulation of the sensory nerves of the bladder. This theory has received general acceptance, and its validity has been substantiated by the work of the recent contributors to the subject.

The normal voiding reflex is initiated by a conscious sensation of fullness which stimulates the sensory nerves of the bladder. The amount of urine necessary to induce this sensation of desire to void is not constant but varies greatly in the same or different persons. The determining factor is the intravesical pressure rather than the volume of urine in the bladder. The threshold of intravesical pressure is dependent on the degree of irritability manifested by the bladder walls.

Graves and Davidoff have made a comprehensive study of the response of the vesical musculature to normal distention. Their studies reveal that the filling of the bladder is not a passive act but rather a distinct muscle activity as characterized by rhythmic wavelike contractions. These contractions are feeble as filling begins but become more marked as the degree of distention increases. The contractions do not invoke a conscious sensation or desire to void until the upper limits of bladder distention are reached. When the maximal intravesical distention is reached all rhythmic contractions cease and there develops a tonic sustained contraction of the bladder walls on its contents. It is at this point that micturition normally takes place. There-

authors point out that during the period of gradual filling, the bladder response is immediate and is manifested by an increase in the length of the muscle fibers without materially changing the tension. When the bladder distention approaches the maximal capacity, the response is isometric as the fibers maintain the same length and respond to stretching force (distending fluid) by a rapidly increasing intravesical tension. Thus it is that the intravesical pressure is the controlling factor in urination, for the maximum capacity of the bladder at a given time is solely dependent on the tone of the musculature. Micturition ensues only when the sustained contraction of the bladder wall has attained a certain degree of intravesical tension.

The foregoing facts have been substantiated by Rose in his recent cystometric studies. He noted that as the normal bladder was filled at a constant rate there was a gradual increase in the intravesical pressure to the point of sensation of the first desire to void. At this point the volume of fluid in the bladder varies from 125 to 175 cc with an average pressure of from 5 to 15 mm of mercury. If the filling of the bladder is continued beyond this point, the intravesical pressure rises more rapidly until the patient expels some of the fluid around the catheter, or until the point of normal contractibility of the bladder is overcome, at which time the pressure mounts very rapidly from 40 to 65 mm of mercury and the patient then complains of severe pain until relieved. It has been frequently observed that a rapid filling of the bladder through a cystoscope or catheter or the use of irritating solutions will induce an imperative desire to void before the desired volume of fluid has been introduced. Likewise, rapid diuresis will cause frequent micturition through a stimulation of the bladder musculature by a smaller amount of fluid than normal.

When the bladder is empty or is undergoing gradual distention the bladder musculature (detrusor) is in a state of relaxation and the internal sphincter is in a state of tonic contraction controlled by the true sympathetic fibers (hypogastric nerves). As the bladder undergoes complete distention and the intravesical pressure increases, the rhythmic contractions of the bladder walls give rise to afferent impulses which pass chiefly by way of the pelvic nerves to the sacral portion of the cord (and perhaps to a lesser extent by hypogastric nerves to the twelfth thoracic and first lumbar segments) and thence to the higher cranial centers. These afferent impulses are increased as the bladder becomes fully distended and emptying of the bladder takes place as the result of reflexes set up in the lower sacral cord. These stimulate the sacral parasympathetic fibers of the nervi erigentes supplying the bladder and thus cause a contraction of the bladder wall and a relaxation of the internal sphincter. This reflex emptying of the bladder is accompanied normally by a voluntary effort which is the result of

afferent impulses from the distended bladder reaching the cerebrum and giving rise to the conscious desire to void. They also give rise to efferent impulses which cause a contraction of the abdominal and respiratory muscles thereby increasing intra-abdominal pressure and aiding in the contraction of the bladder.

The contraction of the abdominal walls, however, is not an essential part of the act of urination, for the emptying of the bladder may be entirely reflex depending solely on the intravesical pressure. When the intravesical pressure reaches from 20 to 30 mm of mercury, the bladder will contract and force the urine through the vesical orifice and urethra. The reflex emptying of the bladder may be inhibited under certain conditions as the bladder is very sensitive to reflex stimulation of psychogenic or sensory origin, which may produce considerable and continual changes in the size and tension of the bladder. It is well known that stimulation of any sensory peripheral nerve will cause a contraction of the bladder. The thought of voiding, the sound of running water, emotional states (fear, fright, anger, etc.) may induce a desire to urinate when the bladder contains but little urine. In such instances, if micturition is prevented by a voluntary contraction of the striated muscles about the posterior urethra, the bladder may relax and the attendant sensation of fulness with the desire to void will pass away until the urine accumulates within the bladder to a point where the intravesical pressure causes a normal sensation of fullness and a desire to void. In other instances, urination may occur before the bladder has accumulated enough urine to initiate the emptying reflex, either by voluntary effort or by virtue of sensory impulses originating in the other parts of the body and affecting the spinal centers in the same way that impulses from the bladder do.

*Other Mechanisms of Urination*—In the foregoing pages we have described in detail the normal mechanism of urination which results from voluntary effort acting on the spinal centers and reinforced by the contraction of the skeletal muscles. In addition to this mechanism two other mechanisms will be considered: (1) intrinsic bladder mechanism (as in the Goltz and Ewald dogs), and (2) reflex automatic bladder resulting from visceral afferent and efferent impulses.

*Intrinsic Bladder Mechanism* This system of bladder-emptying naturally infers an automatic nervous apparatus confined within the bladder walls, i. e., intrinsic nerve plexus. Von Zeissl (quoted by Kretschmer) was able to isolate completely the bladder of dogs from all nerve connections with the central nervous and autonomic systems and found that after an interval they were able to retain their urine and to urinate. Goltz and Ewald removed the lumbar and sacral segments of the spinal cord in dogs and observed that after a primary but temporary retention of urine the dogs gradually developed an auto-

matic contraction of the bladder and in a few months were able to urinate regularly and periodically. Graves pointed out that such automaticity must be attributed to the inherent properties of the bladder muscle fibers which are most likely controlled by the intrinsic nerve plexuses which exist throughout the vesical musculature. Stirling (quoted by Graves) stated that in a bladder severed from its connections with the central nervous system, the automatic rhythmic contractions caused by the accumulation of urine in the bladder gradually increase in force until one of the contractions is able to overcome the resistance of the tonically contracted internal sphincter. Although urination follows in such cases, the bladder is not completely emptied as the intra-vesical pressure falls rapidly to a level too low to maintain the patency of the internal sphincter. Consequently, there is always some residual urine. The intrinsic automatic bladder may follow a complete transverse lesion of the spinal cord below the level of the twelfth thoracic segment, and clinically, is encountered in cord tumors, injuries of the cord, varicose veins of the cord, degenerative lesions of the cord, local arachnoiditis, etc., where the lumbosacral portion of the cord is involved.

**Automatic Reflex Bladder.** This type of emptying mechanism is purely involuntary, since it is operated from the cord (fig 2). There is a complete dissociation of the voluntary portion of the normal emptying mechanism operated from the cerebrum, for as long as cerebral connections with the bladder are intact, an automatic reflex bladder is impossible. Automatic reflex micturition is possible, provided the reflex centers in the spinal cord are preserved and functioning. The automatic reflex bladder is the functional emptying mechanism in infants and is considered a part of the primitive mass reflex system. Following injuries to the spinal cord and disease of the cord above the level of these reflex centers, the bladder is no longer under volitional control. In other words, transverse lesions of the cord below the level of the red nucleus as far down as the level of the twelfth thoracic or first lumbar spinal segments results in the establishment of an automatic reflex bladder and is usually associated with flexor spasms and sweating below the level of the lesion. The amount of urine that the bladder can hold under such conditions varies, but usually is about from 200 to 250 cc. However, this mechanism of automatic emptying of the bladder is dependent mainly on the intrinsic activity of the bladder musculature and frequently proves inefficient due to a maladjustment of the reflex mechanism accompanying the shock of an injury to the spinal cord. In such cases, the urine accumulates until the intra-vesical pressure is great enough to force open the internal sphincter allowing the urine to dribble out feebly, and as a result the bladder is incompletely emptied and a varying amount of residual urine is left behind as a focus for infection.



It is interesting to note that incomplete transverse lesions (1) of cerebral origin tumors, cysts, aneurysms, eye strain, strabismus, circumscribed arachnoiditis, etc., (2) of cerebellar origin tumor, cysts, hemorrhage, etc., (3) of vestibular origin ear and canal lesions and (4) of spinal origin tabes, syringomyelia, etc., are never associated with an automatic reflex bladder but may and often do result in incontinence enuresis and retention. McClintic stated that local organic nerve lesions or irritations may cause a spastic bladder (so-called vagotonia) enuresis and incontinence. Head maintained that irritation of the parasympathetic nerves is the cause of bed-wetting, an incontinence of urine frequently associated with the desire to void, whereas stimulation of the sympathetic nerves causes a paradoxical incontinence (large residual with overflow).

*The Rôle of the Internal and External Vesical Sphincters in Maintaining Bladder Closure*—It is of more than passing interest to note the progress of investigation into the normal functions of the vesical sphincters. A review of the literature on the subject reveals many conflicting opinions as evidenced by the fact that at various times the normal control of miction and mechanism of retention of urine has been attributed to either the internal or external vesical sphincter.

The contention that the internal vesical sphincter can voluntarily control miction by maintaining bladder closure has now been definitely established by experimental, roentgenologic and operative observations. Rehfisch, in 1897, was the first to prove that the internal sphincter is capable of voluntary contraction. He introduced a metal catheter into the posterior urethra, so that its opening was beyond the external sphincter but not quite up to the internal sphincter, and noted that the patient could control voiding perfectly. Prior to this, Born, by his plaster of paris injections of the bladder in cadavers, and Barkow, Henle and Kohlihausch, by their anatomic studies of the vesical neck, considered the internal sphincter the point of normal closure of the bladder although they differed as to the exact structure of this sphincter.

Further confirmation of the normal function of the internal sphincter in maintaining closure of the bladder was obtained by the roentgenologic studies of Voelcker and Lichtenberg in 1907. They filled the bladder with 5 per cent collargol and showed that the internal sphincter maintained closure of the fully distended bladder and at the same time they showed that the outline of the normal bladder was pear-shaped being broad above and narrowed down at the vesical neck. They were unable to show a funnel-shaped formation with obliteration of the internal vesical sphincter when the bladder was fully distended. Other investigators (Leedham-Greene, Baringer and MacKee, Uhl and MacKinney and Hyman) working along similar lines and using the same or different opaque mediums in the bladder confirmed these

results. However, one notes a difference of opinion as to the shape of the bladder when fully distended. Baringer and MacKee, and Hyman have confirmed the observations of Voelcker and Lichtenberg, whereas Leedham-Greene and Uhle and MacKinney found the bladder to be oval, approaching a round form. Legueu described a reverse type with the bladder broad at the base and narrow at the fundus as characteristic of the normal patient in prone position. Typical cystograms of normal bladders in our studies can be seen in figure 5.

Further support of the ability of the internal sphincter to maintain bladder closure is found in observations on the mechanism of control of urination following various operative procedures. Young has repeatedly pointed out that in a properly performed perineal prostatectomy in which the triangular ligament, compressor urethrae and external sphincter have been retracted along with the transverse perineal



Fig 5—Normal cystograms obtained by injecting from 300 to 350 cc of 35 per cent sodium iodide solution through a soft rubber catheter with the patient in the horizontal position. These cystograms demonstrate the normal point of bladder closure at the internal sphincter in the fully distended bladder. The contour of the bladder approaches a round form.

muscles and in which a small slitlike incision is made into the posterior urethra near the apex of the prostate, it is not uncommon to see the patient regain control of the internal sphincter in a few days. Thus the patient is able to retain his urine within his bladder or to expel it voluntarily from the perineal wound and in some instances even to close the bladder after part of the urine has been passed. Following an external methiotomy (for strictures of posterior urethra) wherein the external sphincter is cut or damaged but the internal sphincter is preserved, normal control of urination ensues and incontinence of urine rarely occurs except in those cases of stricture in which the

internal sphincter is destroyed or damaged by the continuous pressure of urine within a chronic distended bladder.

It appears that there is a unanimity of opinion concerning the adequacy of the internal sphincter in controlling bladder closure in the moderately distended bladder, but a marked diversity of opinion exists concerning the mechanism of bladder closure in the fully distended bladder. Earlier writers, Guyon, Ultzman, Finger, Ruggles and Wilson and McGiath, were of the opinion that the internal sphincter was too weak to maintain closure of the bladder under all conditions. They believed that the internal sphincter was sufficient to close the bladder when moderately distended, but under full distention the internal sphincter was overcome and the compressor urethrae, and presumably the external sphincter, were brought into action to retain the urine within the bladder. They contended that there was a funnel-shaped opening formed in the region of the vesical neck owing to distention of the posterior urethra with urine and an obliteration of the internal sphincter. They contended that in the fully distended bladder there is a shortening of the posterior urethra of from 1 to 1.5 cm. more than occurs in the moderately distended bladder. However, this point has been ably refuted by von Zeissl, who has shown that this shortening is not sufficient to account for placing closure at the compressor urethrae or external sphincter which is situated 4 cm. from the vesical neck, and that the latter distance would be the amount of contraction necessary to place the closure at the external sphincter. The beliefs of these earlier workers were substantiated in part by the work of Oppenheim and Loew on monkeys. The latter workers made roentgenographic studies after injecting a bismuth suspension into the bladder and concluded that the compressor urethrae prevented the escape of urine from the fully distended bladder. Their work, however, was not very conclusive, and has not altered the prevailing and accepted theory that the internal sphincter maintains voluntary control of bladder closure.

For a long time physiologists have argued against this view, maintaining that such a phenomenon would present the paradoxical example of voluntary control of involuntary smooth muscle. That such control may exist is not beyond reason or expectation and finds a counterpart in the voluntary control of the muscles of accommodation of the eye. A likely explanation of the voluntary control of closure of the bladder by the internal sphincter has been aptly put forth by Cecil on the basis that the contraction of this sphincter is due to a "reflex, voluntarily initiated."

The question of the rôle of the external vesical sphincter in maintaining bladder closure has long been a debatable one. It has been contended that the function of the external sphincter in controlling urination after the internal sphincter has been rendered useless by oper-

ative intervention or by continuous dilatation from an enlarging prostate is not the normal function of the external sphincter but merely an abnormal circumstance, the external sphincter having taken upon itself a reflex ability to control urination. In other words, it is nature's method of compensating for a deranged internal sphincter. Nevertheless, it has been definitely established that the external sphincter is capable of maintaining bladder closure by itself for observations during and following suprapubic and perineal prostatectomies show that when the external sphincter is preserved, perfect bladder closure and urination results regardless of whether or not the internal sphincter is preserved or injured beyond repair. Young and Cecil both have pointed out that often following a perineal prostatectomy the internal sphincter is inactive and there is a continuous drainage from the perineal fistula. When the fistula closes normal voiding occurs indicating that the external sphincter has assumed control of urination and bladder closure. Further confirmation of the ability of the external sphincter to maintain bladder closure is found in men with deranged internal sphincters resulting from paralysis from a nerve lesion, for these men do void normally although the posterior urethra may be filled with urine. Roentgenologic studies in animals and men in whom the bladder and vesical neck have been rendered useless by artificial or acquired interference with their nerve supply have also confirmed the ability of the external sphincter to maintain control of urination and the retention of urine. Wallace and Hyman have demonstrated by roentgenograms that the external sphincter was the point of bladder closure after suprapubic prostatectomy.

Perhaps the most conclusive evidence of the ability of the external sphincter to function independently of the internal sphincter has been offered by Young in an experiment supplementing that of Rehfish. He inserted into the vesical orifice of normal men a metal tube mounted on a curved slender rod, thus rendering the internal sphincter functionless. He noted that the men were able to maintain full closure of the bladder by bringing the external sphincter into action and also were able to start and stop their flow of urine at will.

It seems that under normal circumstances the external sphincter supplements the action of the internal sphincter and that its assistance in maintaining bladder closure while very useful is not absolutely essential.

The preponderance of data obtained tends to show first that the normal bladder closure is maintained by the internal vesical sphincter, second that when the internal sphincter is rendered functionless by operative intervention or from long continuous dilatation and stretching by an intravesical enlargement of the prostate the external vesical sphincter is capable of maintaining bladder closure, third, that either the

internal or external sphincter can be rendered nonfunctioning and normal urination and bladder closure made to follow, providing the remaining sphincter is in normal condition

#### THE PATHOLOGY OF INCONTINENCE

The pathology of urinary incontinence following prostatectomy is still in its inceptive stage, although recently a considerable amount of new information has been obtained through the studies of Wade, Hyman Cecil Watson, Herman, Walker, Gordon and Denslow. There still exists an imperfect understanding of the readjustment of the musculature of the vesical neck following operative intervention.

It is interesting to note the various explanations for incontinence following prostatectomy that have been offered in the past. In 1901, Woolsey, in discussing three cases of incontinence following perineal prostatectomy reported by Parker Syme, said that incontinence may be partly explained by the injury to the fibers of the prostatic urethra and faulty healing subsequent to the operation. In 1903, Lilienthal explained incontinence on the basis of changes in healing at the neck of the bladder and urethra. He believed that a soft succulent scar at the neck of the bladder and posterior urethra was conducive to a continent bladder, but that a hardened cicatrized scar in this area would lead to a rigid urethra with incontinence. Moore, in 1904, stated that incontinence following prostatectomy is due to injury to the muscles or the nerves or to the neck of the bladder—most often the latter. He also stated that an injury to that "portion of the sphincter of the bladder just below the urethra and in front of the third lobe" (external sphincter?) during operation may result in incontinence. In 1905 Ballenger and Ruggles independently stressed the necessity of avoiding injury to the external sphincter during prostatectomy. Ruggles stated that the derangement of the external sphincter may be due either to an injury to the nerve supply of the external sphincter or to the sphincter itself during the manipulations incidental to removal of the prostatic enlargement especially in the perineal prostatectomy. He wisely suggested that in a perineal prostatectomy the incision into the urethra should be made as close to the prostate as possible and urged extreme caution to avoid stretching and laceration of these muscles.

In 1911, Proust, in writing of the complications of perineal prostatectomy, stated that the mechanism of incontinence is extremely difficult to understand. He pointed out that the vesical neck is not the cause for two reasons. First the hypertrophied prostate causes an eccentric dilatation of the internal vesical sphincter with eventual destruction and second incontinence never occurs after a suprapubic operation where manipulation is confined to the vesical neck and the prostatic urethra. He maintained that incontinence following perineal

prostatectomy is due either to a direct lesion of the membranous urethra or to an injury to its nerve innervation. He expressed the belief that the occurrence of incontinence following perineal prostatectomy is due to the trauma incidental to a difficult operation in removing a very large or firm prostate.

Judd, in 1911, expressed the belief that both the internal and the external sphincter play some part in the control of urine after prostatectomy. He stated that in a perineal prostatectomy it is important to preserve the prostatic capsule, especially in the region of the neck of the bladder, and not to save the elongated and distorted prostatic urethra.

Gardner believed that the preservation of the compressor urethrae muscle following suprapubic or perineal prostatectomy insures a good functional result. He attributed postoperative incontinence to the difficulty associated with the removal of a prostatic obstruction wherein the hyperplastic masses were not easily enucleated. He stated that in such cases injury or partial removal of the aforementioned muscle occurred, and maintained that the injury or removal of the internal sphincter does not have any effect on actual muscular control of urination.

Young (1922), in his article dealing with the operative cure of incontinence, stressed the pathologic structural changes associated with postoperative incontinence following median urethrotomy, perineal and suprapubic prostatectomy. He mentioned the following operative defects: (a) a wide dilatation of both the internal and external sphincters, with incontinence due to lack of function of the external sphincter, (b) wide dilatation of the membranous urethra due to division of the external sphincter posteriorly, (c) postoperative scar tissue in the perineum, and (d) widely dilated internal sphincter with absence of the usual elevation of the median portion and with scar tissue replacing the muscle in that region.

Changes that occur at the vesical neck in cases of incontinence following prostatectomy must necessarily be determined by a study of the surgical pathology of this region. Such a study engrosses the observations recorded at the time of the operation, or after operation with the aid of the cystoscope, urethroscope and x-rays, or at autopsy after operation. Before undertaking a study of the changes associated with incontinence, it is fitting to discuss the structural changes that normally occur after suprapubic and perineal prostatectomy. Walker, Young, Hinman, and Watson have made important contributions to this phase of the subject, and we have drawn frequent references from their work.

*Changes Following the Suprapubic Method*—In the vast majority of cases the readjustment of the musculature about the vesical neck

following this method is manifested by the development of a structural defect, i. e., a cavity formation. The presence of such cavity formation was first noted by Walker in 1904 (quoted by Wallace in 1907), and later clearly demonstrated roentgenographically by Wallace and Page in 1911 and by Hyman in 1914. This cavity is essentially a dilatation of the prostatic urethra following the enucleation of a hypertrophied prostate and results in the prostatic urethra becoming a part of the bladder cavity. The cavity is usually funnel-shaped and quite large, and is accompanied by a widely dilated and functionless internal sphincter. In a few cases the cavity assumes a spindle shape, is not quite as large as in the previous type and is associated with a contracted vesical neck. In the vast majority of cases, the point of bladder closure is at the external sphincter with perfect urinary control as shown by Wallace,



Fig 6—Cystogram in case following suprapubic prostatectomy with excellent functional result. The anatomic defect in the form of an enucleation cavity is clearly defined. Perfect bladder closure is maintained by the external sphincter. This is the type of postoperative cystogram found in the majority of cases of suprapubic prostatectomy.

Hyman and others (fig 6). It is rare to find the internal sphincter restored and functioning after suprapubic prostatectomy, for the internal sphincter is practically always destroyed or rendered useless by the trauma incidental to this method of enucleation. Examination of the bladder cavity at varying intervals after operation reveals a persistently relaxed internal sphincter. In figure 7 a cystogram following a suprapubic prostatectomy in one of our cases is shown. The point of bladder closure appears to be at the internal sphincter, but when closely examined it is noted that some dye leaks into the enucleation cavity. Perfect closure is thus maintained by the external sphincter. In this case the internal sphincter was only partially injured

at the time of operation and hence there is a partial restoration of function of this sphincter after operation

The development of a cavity following suprapubic prostatectomy is dependent on two factors (1) anatomic changes produced by the enucleation of the prostate and (2) method of packing for controlling hemorrhage. In the hands of the ordinary suprapubic surgeon the enucleation is essentially a blind procedure with division and injury to the internal sphincter. Since the prostate is normally an extra-vesical and extra-urethral organ subcapsular enucleation necessarily requires a division of the internal sphincter before the enlarged mass can be shelled out. In removing the hypertrophied tissue, particularly the portion that pushes up under the base of the bladder, the mucous membrane of the bladder about the vesical neck together with the



Fig 7—Cystogram in a case following suprapubic prostatectomy in which no incontinence was present. The point of bladder closure is observed at the internal sphincter, except for a small amount of dye which leaked into the enucleation cavity. Absolute bladder closure is maintained by the external sphincter.

dilated internal sphincter is stripped back for some distance. In many instances, complete divulsion of the prostatic urethra is produced unintentionally and leaves a large denuded gap between the bladder and anterior urethra. The manipulation of the finger in the posterior urethra and within the prostatic capsule may cause a varying amount of damage to the intrinsic musculature of the prostatic urethra. The latter musculature when preserved after operation may play an important part in assisting the preserved external sphincter to maintain perfect bladder closure after suprapubic prostatectomy. These anatomic changes aid in altering the shape of the prostatic urethra and bladder by producing a temporary loss of tonicity of the musculature about the vesical neck and by delaying healing of the structural defect about



the prostatic urethra which results from operation and which causes a break in continuity between the bladder and anterior urethra

To control hemorrhage in the suprapubic operation, the prostatic bed is packed very tightly from above either with gauze or a rubber (Pilcher) bag or a smooth metal cone. Thus the prostatic urethra is dilated and elongated and tends to produce a marked separation of vesical neck from the enucleation cavity. Such a cavity would naturally be exaggerated should repacking be required.

Nevertheless the existence of a cavity does not interfere with or prevent perfect miction, provided the integrity of the external vesical sphincter is preserved. When a disturbance of miction, such as retention or incontinence, does occur after suprapubic prostatectomy, it is practically always due to permanent injury to the external sphincter or to some mechanical intervention with the function of this sphincter or the internal sphincter in the form of loose fragments of prostatic urethral or bladder tissue producing a ball-valve obstruction, or to a narrowing of the lumen of the vesicoprostatic orifice produced by stricture, bar or canopy formation. However, the occurrence of such unfavorable structural defects within the enucleation cavity has been greatly decreased by the recent advances in the technic of the suprapubic operation whereby the uncertainty of blind enucleation with the finger has been replaced by accurate dissection in a clearly visualized operative field. Hemorrhage at the time of operation has been controlled more completely by ligation of bleeding vessels and by suturing the torn prostatic capsule and vesical wall than by trusting to the uncertainty of gauze packs.

*Changes Following the Perineal Method*—Watson studied the mechanism of bladder closure following perineal prostatectomy and pointed out that there is an early readjustment of the musculature about the vesical neck. The point of bladder closure in practically every instance is found to be at its normal site, i. e., the internal vesical sphincter. The external sphincter should be preserved in every instance following a properly performed perineal prostatectomy. The restoration of function in the internal sphincter may take place as early as three days after operation as manifested by the ability of some patients to maintain bladder closure with perfect urinary continence for one or two hour intervals. The return of function to the internal sphincter is usually complete by three weeks after operation and persists throughout life.

In figure 8 are shown cystograms taken before and after perineal prostatectomy. In the preoperative cystogram (*Pre-O*), the point of bladder closure is at the internal vesical sphincter. Intravesical bulging of the prostate and a small diverticulum are also shown in this picture. In the postoperative cystogram (*PO*) the bladder has assumed an

oval outline with some of the dye leaking into the enucleation cavity. The point of bladder closure is at the external sphincter. These cystograms are the usual ones found in a continent bladder following a perineal prostatectomy where some damage to the internal sphincter occurs at operation but the external sphincter is preserved.

There is usually no cavity formation following a properly performed perineal prostatectomy where the internal sphincter is preserved but other anatomic and structural changes about the vesical neck may occur which may cause some interference with urination. It is generally conceded that incomplete and irregular enucleation of the prostatic mass, especially in cases with subtrigonal involvement, is more likely to occur after the perineal method than after the suprapubic method. In some cases, the obstruction to passage of urine may be due to loose portions of prostatic tissue and prostatic capsule left behind after incomplete enucleation of the prostate, in other cases,

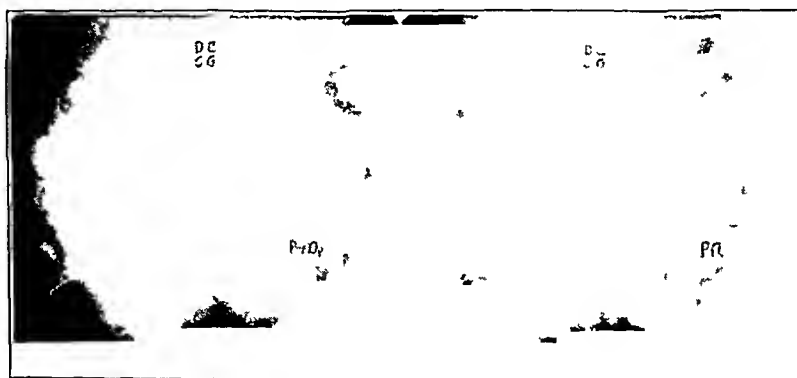


Fig 8—Preoperative (*Pre-O*) and postoperative (*P O*) cystograms in a case of perineal prostatectomy with a continent bladder. The point of bladder closure is at the internal sphincter in the postoperative cystogram. In the latter picture, partial closure is noted at the internal sphincter with some dye in the enucleation cavity. This may be explained by partial injury to the internal sphincter at the time of operation.

deep fissure formation in the posterior urethra or plication of redundant urethral walls may follow the removal of a large adenomatous prostate with marked intra-urethral bulging.

When incontinence does follow a perineal operation it is always accompanied by some injury to the sphincteric musculature about the vesical neck and posterior urethra. Such a complication should not occur as frequently as it does for the perineal removal of an enlarged prostate is essentially an extra-urethral and extravescical operation wherein the hypertrophied mass is shelled out of its capsule leaving both vesical sphincters intact. However in the hands of an inexperienced surgeon some damage may be done to the vesical sphincters and to the intrinsic musculature of the posterior urethra in carrying out a

perineal dissection. Injury to the external vesical sphincter can be avoided by making the external urethrotomy incision (for the introduction of the Young's prostatic tractor) at a point below the external sphincter, preferably near the apex of the prostate. This potential danger may also be obviated by omitting the introduction of the Young's prostatic tractor through an incision of the membranous urethra and using a long prostatic tractor which is passed through the external meatus of urethra into the bladder as advocated by Geraghty, Cecil and Morrissey. Unquestionably, prolonged traction on the prostate with such instruments can also damage the internal sphincter. Traction with the Young prostatic tractor should be in an upward and outward direction to avoid further lengthening of the urethrotomy incision anteriorly with subsequent injury to the external sphincter.

As the field of operation in a perineal prostatectomy is constantly under control of the eye, a careful dissection of the perineum can always be carried out, minimizing the traumatization and derangement of the musculature about the vesical neck. The absence of cavity formation after the perineal operation may be attributed to the method of packing the enucleation cavity to control hemorrhage. Hemostasis in the perineal operation is dependent on an intraprostatic compression which is maintained by packing the prostatic cavity lightly with gauze from below, in contradistinction to the suprapubic method of controlling hemorrhage by an intra-urethral compression of prostatic cavity from above with subsequent pouchlike dilatation of the enucleation cavity. In the perineal method, the gauze packing within the prostatic cavity is always extra-urethral and tends to compress and obliterate the enucleation cavity. Recently, Young has adopted the use of a Davis rubber bag inserted into the bladder for drainage and hemostasis and the principles of its hemostatic action are essentially the same as suprapubic method of intra-urethral compression of the enucleation cavity. It is possible for the cavity formation to occur after such a procedure.

Recently the authors have advocated a new technic for perineal prostatectomy in which gauze packs are placed in the prostatic bed between the prostatic capsule and urethral wall for hemostasis only. These are placed against an indwelling catheter placed in the bladder by way of the urethra. The catheter is used for urinary drainage during the convalescence, avoiding the perineal drainage.

By this method the cavity formation mentioned, which is usually formed in the other methods of prostatectomy, is here avoided. We believe that this cavity formation tends to damage or to distort the internal vesical sphincter in a certain percentage of the cases if it is not already damaged during the removal of the prostate.

## CAUSATIVE FACTORS OF INCONTINENCE

It matters little which method of prostatectomy has been used, the incontinence of urine resulting from such an operation in every instance is due to a loss of function of both sphincters. As has been previously stated, either the internal or the external sphincter is capable of maintaining excellent control of urination in the event of the loss of function of the other.

The usual operative defect associated with incontinence is a wide dilatation of both the internal and the external sphincter, accompanied by a dilatation of the membranous and posterior urethra. The muscular components of the internal and the external sphincter are replaced by scar tissue. In the region of the internal sphincter, the usual prominence of the median portion is absent, due to the replacement of the injured muscles by scar tissue.

Our investigation, as well as the observations of others, of the vesical neck and posterior urethra in cases of urinary incontinence following prostatectomy reveals various types of anatomic defects or pathologic lesions associated with the loss of function of the internal and external sphincters. These associated changes about the vesical neck or posterior urethra per se do not cause urinary incontinence but may increase the urinary difficulties as a result of the altered urinary passage and hence may be considered as contributory factors. These changes or defects do occur in a large percentage of the cases and for all practical purposes may be divided into intrinsic and extrinsic groups. In the intrinsic group, which comprises by far the largest number of cases, the anatomic defects associated with urinary incontinence are the result of some structural change at the vesical neck or posterior urethra following operation. The extrinsic group is composed of a very small number of cases in which the urinary disturbance is due to some preexisting lesion or anatomic change in structure which persists after operation and interferes with the proper function of the internal and external sphincters. We wish to stress the fact that the occurrence of many of these anatomic or pathologic changes of either the intrinsic or the extrinsic group, in the presence of one or both good functioning sphincters has a tendency to produce an obstruction to urination with a resultant retention rather than urinary incontinence. Our studies justify the following classification:

*Urinary Incontinence Following Prostatectomy*

## Etiology

Temporary or Permanent Derangement of the Internal and External Vesical Sphincter

Associated Changes or Contributory Factors

*Intrinsic Group*

Loose Tissue Flaps at the New Vesical Orifice

(a) Strips of Mucous Membrane of the Bladder

(b) Nodules of Prostatic Tissue

(c) Strips of Prostatic Capsule

(d) Strips of Urethral Wall

(e) Plication of the Urethral Wall

Strictures or Contractions at the Vesicoprostatic Orifice

(a) Canopy Formation

(b) Bar or Ledge Formation

Stricture in the Region of the External Sphincter

Deep Fissure or Sulcus Formation in the Posterior Urethra

Complete Divulsion of the Prostatic Urethra

*Extrinsic Group*

Hypertrophy of the Trigone

Intravesical or Prostatic Tumors

Vesical Calculi

Atony of the Bladder    Preeexisting Nerve Lesions Involving the Mechanism of Urination

Diverticulum of the Bladder

Urethral Lesions (Stricture, Calculi and Tumor)

A brief discussion of the rôle of each factor in the development of postoperative urinary incontinence is in order

## ETIOLOGY

*Temporary or Permanent Derangement to the Internal and External Vesical Sphincters*—Many authorities, particularly Walker in writing on the suprapubic and Young on the perineal method, have repeatedly stressed the absolute necessity of preserving the integrity of the vesical sphincters at the time of operation. Their reasons are obvious, since the internal and external vesical sphincters play the most important part in the mechanism of urination and in the maintenance of perfect bladder closure. In many instances the internal sphincter has already been rendered functionless by the enlarging prostatic adenoma before the patient seeks relief by operative intervention.

The pathologic anatomy of the benign hypertrophied prostate is such that as a rule the adenoma is found on the floor and sides of the posterior urethra. As these adenomatous areas continue to enlarge, the posterior urethra lengthens and the internal vesical sphincter is gradually dilated and stretched especially as the growth pushes through into the lumen of the bladder. Very often the internal sphincter surrounds and grasps this enlarging adenomatous mass (so-called median lobe hypertrophy) about the waist or central portion so that the upper part of the enlarged gland comes to lie free in the bladder in front of the trigone presenting the well known intravesical bulging. In many

cases, the portion of the adenomatous gland below the constricting internal sphincter may bulge inward thus narrowing the lumen of the prostatic urethra and producing the intra-urethral bulging so commonly observed. In the majority of cases, the internal sphincter is temporarily deranged and perhaps in a few cases permanently destroyed when such a condition exists at the time of operation. Consequently, the operator is required to exercise caution to preserve the remaining functioning sphincter (i e., external sphincter) to insure a good result and to avoid that dreaded bugbear, incontinence.

The proponents of the suprapubic prostatectomy assume that in those cases in which the hypertrophied prostate is removed without wounding the dilated internal sphincter, this sphincter will eventually regain its tone. The question arises: Is the hypertrophied prostate capable of being removed by the suprapubic method without injury to the internal sphincter at some stage of its enucleation? This seems well nigh impossible when one recalls that the prostate is an extravesical organ and that removal by the transvesical approach necessitates a further stretching of an already dilated internal sphincter and division with possible destruction of the internal sphincter. The fact remains, however, that the probability of damaging the external sphincter during a suprapubic enucleation is remote, for the field of operation is confined to an area above the triangular ligament. Hence, one is insured of at least one good functioning sphincter with an ultimate good operative result from the standpoint of urinary continence, for it has been definitely established by Wallace, Hyman and others that the external sphincter is sufficient and does maintain perfect bladder closure after suprapubic prostatectomy.

Young has repeatedly pointed out that injury to either vesical sphincter should never occur during a carefully performed perineal prostatectomy, which calls for (1) retraction of the triangular ligament, external sphincter and transverse perineal muscles, (2) an extra-urethral removal of the hypertrophied gland leaving the internal sphincter and most of the posterior urethra intact and (3) introduction of Young's prostatic tractor through an incision made below the external sphincter preferably at a point near the apex of the prostate. Nevertheless, there always remains the potential danger of injuring the internal sphincter by prolonged traction with the Young tractor or damaging the fibers of the external sphincter and compressor urethrae muscle in carrying out a dissection of the perineum. It is in the hands of the inexperienced surgeon not fully acquainted with the operative details and technic of the procedure that many of the disparaging cases of incontinence have occurred and perhaps accounts for the unpopularity of this method.

## ASSOCIATED CHANGES OR CONTRIBUTORY FACTORS INTRINSIC GROUP

*Loose Tissue Flaps or Tags About the New Vesical Orifice—*

Examination of the prostatic cavity after operation often reveals loose masses of tissue (fig 9) in or about the vesicoprostatic orifice which may interfere with urination. The examiner frequently is at a loss to explain the presence of these loose masses following what he believes to be a perfect enucleation. This type of structural defect is seen most frequently after the suprapubic method. Thomson Walker has written extensively of this type of lesion, and owing to his persistent and untiring efforts, genito-urinary surgeons have become better acquainted with its signs, symptoms and treatment.

Total subcapsular enucleation of the gland by sharp and blunt dissection is practically impossible and consequently loose fragments of

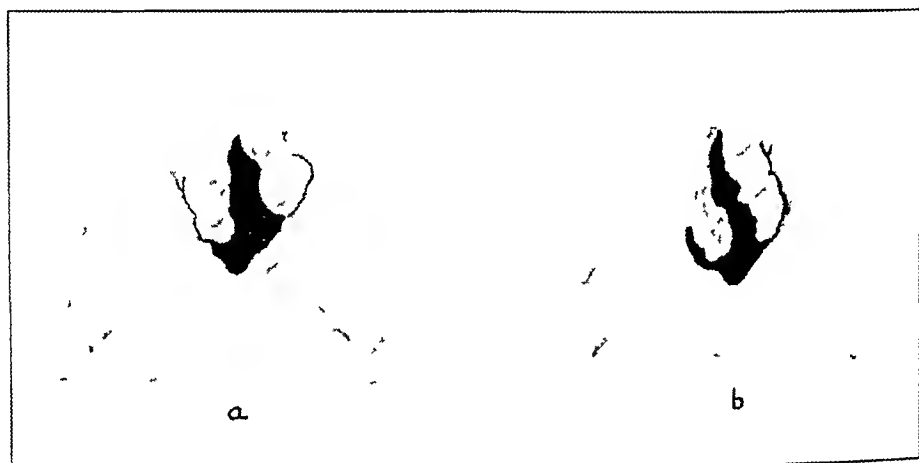


Fig 9—Anatomic defects at vesical orifice following suprapubic prostatectomy. *a*, nodules of prostatic tissue at the prostatovesical orifice, *b*, strips or tags of mucous membrane at the prostatovesical orifice. (Drawing after Walker Brit J Surg 7 530, 1920.)

prostatic capsule and small nodules of the prostatic adenoma may be left behind, especially if a blind operation is performed. These loose strips of capsule and small nodules of gland tissue are usually loosely attached to the wall of the prostatic cavity and as a rule slough away, but occasionally they persist and encroach on the new vesical opening causing a ball valve or polyp-like obstruction which permits a small amount of urine to escape through the contracted orifice.

The presence of loose flaps of mucous membrane of the bladder is not infrequently encountered. After suprapubic enucleation of the adenoma the prostatic bed contracts practically at once but often not quite enough to close entirely the opening between the bladder and the anterior urethra; consequently there may be left behind on the posterior surface of the bladder one or more unsupported crescent-shaped flap-

of bladder wall with a raw edge and with the dilated internal sphincter attached thereto. This defect is found mainly in those cases in which the adenomatous mass has extended up under the trigone. It is rare to find a loose anterior flap of bladder wall even in those exceptional cases in which there is an enlargement of the anterior lobe. These loose flaps of bladder wall may interfere with urination by acting as a mechanical irritant or by meeting over the prostatic cavity and blocking the newly formed vesicoprostatic opening, causing a permanent or intermittent obstruction. Often these loose flaps may slough away and effect a spontaneous cure, or they may become impregnated with urinary salts and give rise to hard calcareous masses or in some instances to bladder calculi. These loose tags also act as a nidus for harmful bacteria.

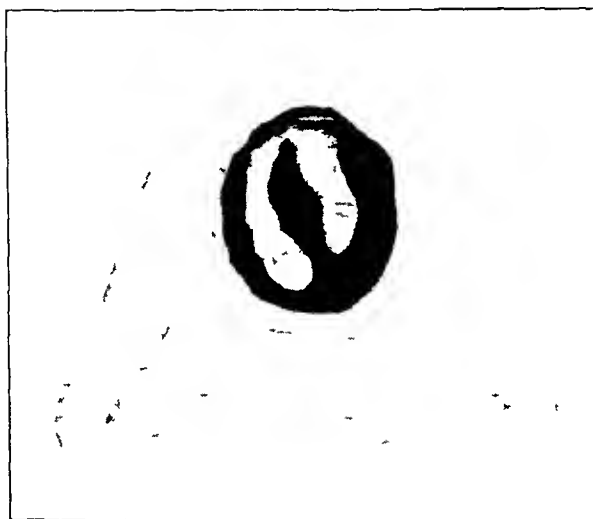


Fig. 10—Loose strips of urethral mucous membrane or prostatic capsule in the enucleation cavity. (Drawing after Walker. *Brit J Surg* 7 534, 1920.)

and serve as a causative or stimulative agent for a persistent post-operative cystitis.

Long loose strips of the posterior urethra wall (fig. 10) coursing the length of the prostatic bed or strips torn across in a transverse direction may occur after the removal of a prostate. They are the results of the tugging and pulling incidental to blind enucleation by the suprapubic method. Such a defect is likely to follow the removal of a hard fibrous prostate.

Mucosal plications may be present and may lead to interference with urination and obstruction to instrumentation. This type of defect is seen most frequently after the perineal operation in cases of large hypertrophied prostate with marked intra-urethral bulging. In these cases the adenomatous tissue is removed extra-urethrally, leaving redundant hypertrophied walls of the urethra free to sag and meet in the



lumen of the posterior urethra, forming a valvular depression (fig 10) and thus interfering with proper emptying of the bladder

*Structure or Contractions at the Vesicoprostatic Orifice*—Canopy Formation (Figs 11 and 12) This type of anatomic defect occurs most frequently following suprapubic prostatectomy, and may occasionally be associated with urinary incontinence. Thomson Walker has pointed out that stricture formation after prostatectomy is likely to occur at the vesical neck and at the membranous urethra where the mucous membrane of each is severed or torn across during the process of enucleation. The most frequent site for the occurrence of stricture or stenosis is at vesicoprostatic margin. Here the edges of the torn bladder

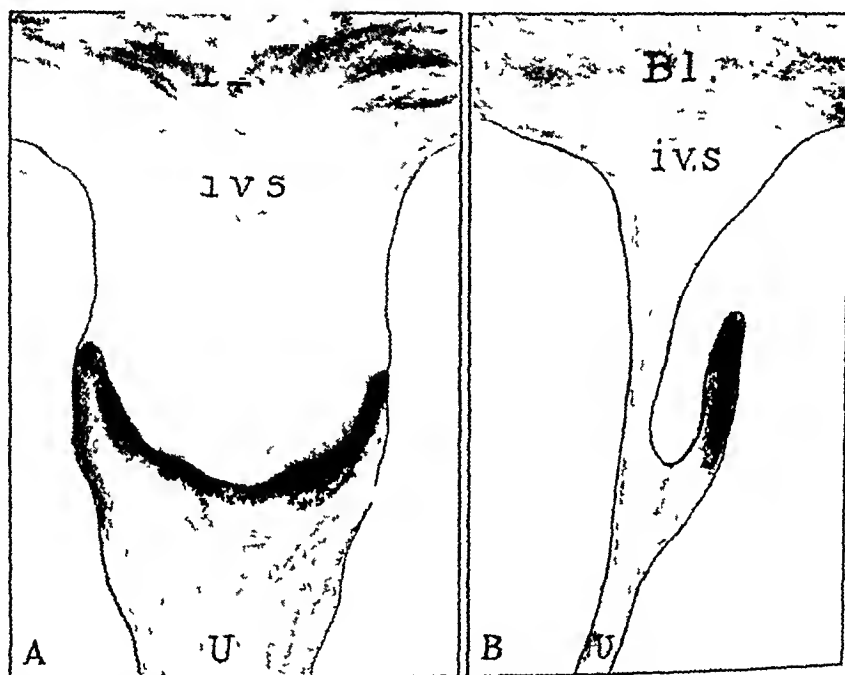


Fig 11—Redundant posterior urethral wall forming a valvular depression in a case of incontinence observed by the authors. This patient had a perineal prostatectomy performed at another hospital. *A* shows the posterior view, *B*, the sagittal view, *Bl.* indicates the bladder, *i.v.s.*, the internal vesical sphincter, *U*, the posterior urethra.

mucosa posteriorly and laterally tend to grow together and form a canopy or tympanum which shuts off the prostatic cavity from the bladder. In those cases in which the hypertrophied prostate is removed by intra-urethral manipulation without completely injuring the dilated internal sphincter the sphincter may regain its tone within a week, and as the contraction progresses, the sphincter is drawn together in the manner of a purse string, narrowing the vesical outlet.

It appears that in the majority of cases the internal sphincter will normally contract more readily than the remainder of the enucleation

cavity and regain its tone quickly as the component circular fibers of the injured or weakened sphincter gather strength. It is in the rare case that the degree of contraction of the internal sphincter is marked, so that the resultant vesicoprostatic opening becomes narrowed and often sclerosed by the increasing amount of fibrous components of the internal sphincter which occurs during the process of healing.

If one were to inspect the bladder in a case with canopy formation, one would find the vesical orifice presenting itself either as a small opening, a dimple or a bud of granulation tissue located well forward near the anterior wall of the bladder. As a rule, the anterior lip of the opening is represented by a very slight ledge where the bladder wall

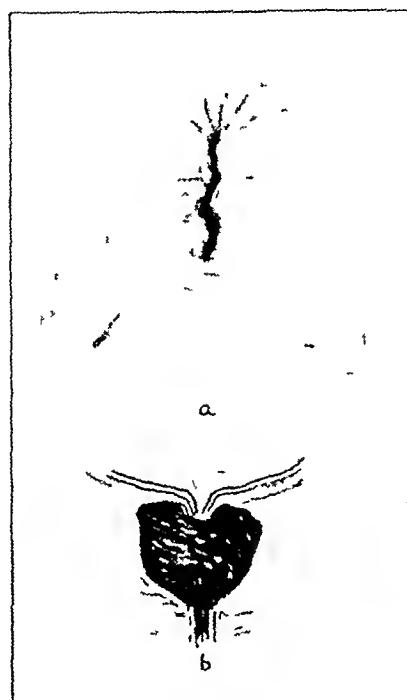


Fig 12—Canopy formation over enucleation cavity following suprapubic prostatectomy as a result of union of the lateral folds. *a*, view from the bladder, *b*, sagittal section. (Drawing after Walker. Brit J Surg 7 529, 1920.)

becomes continuous with the urethral wall. The posterior lip is formed by a hard, fibrous, crescent or sickle-shaped fold. The formation of this diaphragm is dependent on the drawing up of the lower segment of the bladder by contraction of the internal sphincter, thus preventing a natural coalescence of the mucous membrane of the bladder and anterior urethra within the enucleation cavity.

On passing a sound or catheter through the urethra in such cases, one experiences great difficulty in finding the opening on the tympanum even with the aid of a finger in the bladder. One is easily misled to believe that the instrument is in the bladder whereas it is merely

pushing up on the tympanum like a tent pole. As Gordon has pointed out the enucleation cavity beneath the canopy is often large enough to permit the complete rotation of a short beaked sound within it. The difficulty in introducing the instrument may be attributed to a failure of the posterior urethra to serve as a guide because of the misalignment of the posterior urethra with the opening in the tympanum.

The incidence of such canopy formation is fortunately rare. Its relative infrequency is perhaps due to the fact that in most cases the internal sphincter has been sufficiently injured at the time of operation and its healing delayed long enough to permit a natural coalescence of the mucosa of the bladder and anterior urethra.

**Bar or Ledge Formation (Fig 13)** In some cases of urinary incontinence following prostatectomy, more so after the suprapubic than

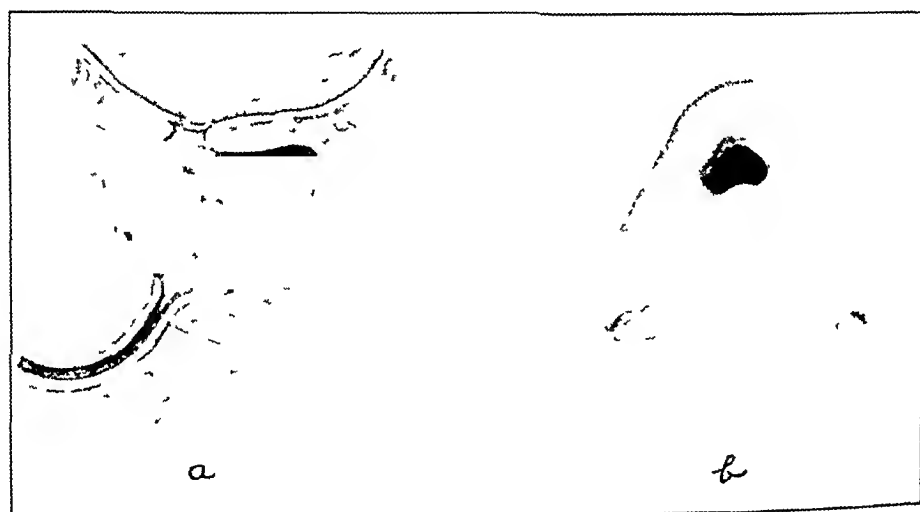


Fig 13—Canopy formation at prostatovesical orifice resulting in unusual healing of posterior wall of bladder. The opening into the bladder is situated at the anterior aspect of enucleation cavity. *a* shows the sagittal section, *b*, the view from the bladder. (Drawing after Walker Brit J Surg 7 529, 1920)

after the perineal method, there may be found at the posterior lip of the vesicoprostatic orifice either a transverse bar or a raised crescent-shaped ledge which tends to narrow the lumen of the opening and interferes with the emptying of the bladder. This bar or ledge is formed by the trigone and parts of the continuous posterolateral walls of the bladder plus a part of loosely attached internal sphincter. The formation of this type of defect is due to the trauma incidental to the enucleation of a large intra-urethral prostate with subtrigonal enlargement.

**Stricture in the Region of the External Sphincter**—Stricture formation at the anterior end of the prostatic bed with resultant marked dilatation of the prostatic bed and bladder is theoretically possible but actually rare. Such a complication should never occur after a supra-

pubic prostatectomy, but could follow a perineal operation when the external sphincter is injured through faulty dissection or from undue traction with the prostatic tractor

*Deep Fissure or Sulcus Formation in the Posterior Urethra*—In some cases of urinary incontinence following prostatectomy, there is occasionally found a deep sulcus or fissure in the floor of the posterior urethra extending from the internal sphincter to the bulb, which interferes with the action of both sphincters. Occasionally the sulcus or depression may take a transverse course across the urethra, especially on the posterior urethral wall (fig 14). This type of lesion occurs most

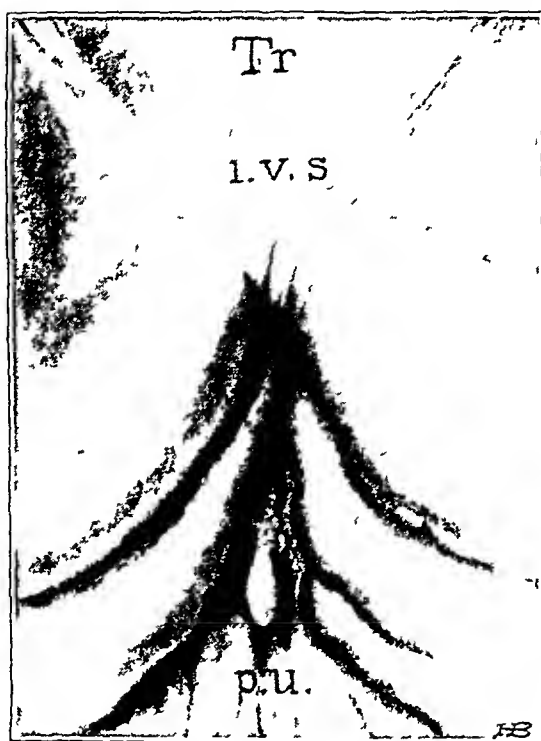


Fig 14—Ledge formation within the posterior urethra due to redundant urethral walls, small nodule of tissue projection on the posterior surface of urethra. This patient was operated on at another hospital and developed complete incontinence. *Tr* indicates the trigone muscle, *I.V.S.*, the internal vesical sphincter, *p.u.* the posterior urethra.

frequently after perineal prostatectomy and perineal operations for strictures of the urethra following gonorrhea, and is due to the trauma and delayed healing following an incision of the posterior urethra. It is possible that in some cases of perineal prostatectomy the traction on the Young prostatic tractor may cause a further gaping of the incision in the posterior urethra. It is also possible that the use of a Davis rubber bag or a rubber tube inserted into the bladder for hemostasis or drainage purposes may produce an exaggerated separation of the fibers

of the prostatic urethra and may lead to delayed healing with ultimate fissure or sulcus formation

*Complete Divulsion of the Prostatic Urethra*—It is commonly believed that the entire prostatic urethra is removed in the suprapubic operation for an intra-urethral hypertrophied prostate, while in one that bulges intravesically the enucleation may be performed without the entire removal of the prostatic urethra. However, such a defect may occur not only during suprapubic prostatectomies but also during perineal prostatectomy when the prostate is removed "en masse." In the majority of cases of this type, the torn edges of the mucosa of the bladder and anterior urethra successfully bridge the gap within a short time and heal without interference with urination. In a very few cases in which the entire circumference of the posterior urethra has been removed, stricture formation has resulted which required postoperative dilatation or another operation to remove the obstruction to urination. Careless removal of the prostate en masse by either method of prostatectomy may cause irreparable damage to both sphincters with resulting incontinence.

#### EXTRINSIC GROUP

*Hypertrophy of the Trigone*—In view of the rôle the trigone normally plays in opening the vesical orifice during micturition, it is not surprising to find a compensatory hypertrophy of the trigone when there is an obstruction of the vesical orifice by an enlarged median lobe. Occasionally, the hypertrophied trigone is seen through the cystoscope as a distinct enlargement behind the vesical neck, but most frequently the hypertrophied trigone forms a firm compact mass with the enlarged prostate. Young pointed out that when the obstruction (hypertrophied prostate) is removed there is often an associated atrophy or diminution in size of the enlarged trigone. As early as 1911, Young stressed the fact that a true hypertrophy of the trigone may exist without an enlarged prostate and present signs of obstruction to urination by acting as a transverse dam in the floor of the bladder. In long-standing cases, the hypertrophied trigone produces a pouchlike depression (*bas fond*), and the latter undermines the trigone and dissects it free from the bladder causing a valvelike obstruction to urination. Such an obstruction might easily be overlooked at operation, and its persistence after operation may interfere with the passage of urine. Thomson Walker was the first to emphasize the rôle that the thickened walls of the trigone played in the formation of ledge or canopy obstructions following suprapubic prostatectomy, and he strongly advised the precautionary measure of removing at the time of operation a wedge-shaped portion of the posterior vesicoprostatic septum as far as its junction with the bladder.

*Intravesical or Prostatic Tumors*—Preexisting papilloma of the bladder may also serve as a valvelike obstruction to urination after operation, and in rare instances may cause an incontinence of an infiltration of the tissue near the vesical neck, thus interfering with the action of the internal sphincter. Occasionally, a nodule or lobe of adenomatous tissue may be left behind at the time of operation, and this may continue to grow and cause some interference with urination.

Another cause of postoperative incontinence is the recurrence or further growth of a carcinoma of the prostate which may not be suspected at the time of operation.

*Vesical Calculi*—Vesical calculi occurring shortly after operation are usually due to the impregnation of loose flaps of bladder or prostatic tissue with the mineral salts of the urine. They usually lead to some degree of ball-valve obstruction at the newly formed vesical orifice and result more often in retention than in incontinence. The calculi may be found in either the bladder or the prostatic pouch but rarely in both. Occasionally, small calculi will be found in the shallow cellules or between trabeculations.

*Atony of the Bladder*—Atony of the bladder walls due to a prostatic obstruction may cause a false incontinence in the sense of an overflow or retention in the nonoperative case. Removal of the hypertrophied prostates in patients with a marked degree of atony may be followed by a temporary and usually partial incontinence. It is generally agreed that atony of the bladder dependent on a prostatic obstruction and incident to old age is not a contraindication to operation, provided the entire obstruction is removed at operation. Incomplete restoration of the tone of the bladder musculature and a small amount of residual urine may follow the complete removal of the prostate in many of the cases.

It is essential to differentiate preoperatively the type of atony of the bladder associated with the prostatic obstruction from the nonobstructive type produced by diseases of the central nervous system. Tabes and cerebrospinal syphilis are the most common causes of the nonobstructive type of bladder atony, and less frequent causes are tumor of the spinal cord or injury, lateral or multiple sclerosis and syringomyelia. The retention that follows a cerebral or spinal lesion may be partial or complete depending on the degree of atony of the bladder walls, and the incontinence that often follows is dependent on the degree of paralysis of the internal and external vesical sphincters. Consequently, all cases of atony of the bladder should be carefully differentiated before operation by cystoscopic, complete neurologic and serologic studies. Otherwise patients with hopeless cases will be submitted to an operation with absolutely no chance for a good functional result. Although the prostate is atrophied as a rule in the presence of a spinal lesion, in rare instances a true hypertrophy may exist. In such cases if the spinal lesion is not

too far advanced and the atony of the bladder is definitely proved to be due to the prostatic enlargement, operative intervention with removal of the obstruction is warranted

*Diverticulum of the Bladder*—A diverticulum of large or moderate size may act as an obstruction to the escape of urine from the bladder and urethra. This type of lesion must be considered in those patients in whom a complete routine study (including cystoscopy and cystography) was not made for any of various reasons

*Urethral Lesions*—The presence of a stricture of the anterior or the membranous urethra, calculi in tumors of the urethra, may possibly serve as a cause of postoperative urinary discomfort, but fortunately such lesions are readily detected preoperatively and successful treatment can be readily instituted

#### REPORT OF CASES

CASE 1—C. H. S., aged 64, was admitted to the Sinai Hospital on Jan. 13, 1927, with a history of marked diurnal and nocturnal frequency. He stated that he had had a sensation of not completely emptying his bladder after voiding. Rectal examination revealed no enlargement of the prostate. On cystoscopic examination, it was noted that there was 100 cc. of residual urine with a capacity of 400 cc. There was only slight bulging of the prostate laterally, but a rather marked median lobe was present. There was practically no intra-urethral bulging. Many cellules and trabeculations were observed. The urine showed a 2 plus sugar reaction.

On February 11, when the urine was free from sugar as the result of diabetic treatment, a one-stage suprapubic prostatectomy was performed. The lateral lobes were fibrotic and difficult to remove. The median lobe was the largest of all and was also fibrotic.

There was delayed healing of the wound, but finally it closed. At the time of discharge from the hospital, the patient was able to void in a good stream and was able to start and stop the stream, but there was some dribbling between and at the end of urination. Treatment was given for this, but no relief was obtained. Six months after the operation, cystoscopic examination revealed marked relaxation of the posterior segment of the vesical orifice. The posterior edge appeared to be drawn up to the ureteral orifices, indicating marked relaxation of the internal vesical sphincter. There appeared to be a small diverticulum in the posterior urethra, just behind the verumontanum.

A cystogram (fig. 15), taken after the injection of 630 cc. of 3.5 per cent sodium iodide, revealed the point of closure to be at the internal vesical sphincter with some dye leaking through the internal sphincter.

A urethrogram, taken after the injection of 20 cc. of 3.5 per cent sodium iodide into the posterior urethra, revealed a slight irregularity but no definite pouch formation.

*Comment*—Partial urinary incontinence in this suprapubic case is the only one in our series although its occurrence is not infrequent with other surgeons. The explanation is simple and its occurrence has been of tremendous value to us for we feel that in our cases it will not occur again in the near future under similar circumstances.

In this case, the bladder had been drained with a catheter for several weeks prior to operation. The history of urinary difficulties plus the amount of residual urine served as the reason for a prostatectomy. At operation, a very small fibrous prostate was found with very slight bulging laterally and a very small median lobe. It was quite a task to remove the fibrous growth from its capsule, and in the manipulations incidental to its removal it is extremely likely that fibers of both sphincters were torn, resulting in incontinence. We believe that the logical procedure in a case of this type in the future is a punch operation performed without opening the bladder or at the operating table when an examination reveals a small fibrous gland.



Fig 15—Cystogram in a case of partial incontinence following suprapubic prostatectomy. The point of bladder closure was at the internal sphincter, but some dye escaped through both sphincters.

CASE 2—S. S., aged 61, was admitted to Sinai Hospital on May 10, 1926. He had the usual symptoms of prostatic enlargement, consisting of diurnal and nocturnal frequency, hesitancy, urgency and dribbling. He had acute urinary retention on several occasions. Rectal examination revealed a very large right lobe with a smaller left one, of a soft and doughy consistency, with no evidence of malignancy. Cystoscopic examination revealed the amount of residual urine to be 60 cc, with a bladder capacity of 300 cc. There was marked intravesical and intra-urethral bulging of the prostate on the right, less marked on the left, with a moderate amount of bulging posteriorly in the form of a median lobe.

On October 29, perineal prostatectomy was performed. The bulb was unnecessarily exposed and an incision was made high in the membranous urethra. The lateral incisions were made in the prostatic capsule and then connected, making it an inverted "U" incision. The prostate was removed en masse, taking the prostatic urethra with it. A catheter was passed into the bladder by way of the



urethra and another into his bladder by way of the external urethrotomy incision. One iodoform gauze pack was placed in each prostatic cavity.

On his discharge from the hospital, four weeks after operation, his perineal wound was closed. He was voiding in a good stream, every one to one and one-half hours during the day and about every two and one-half hours during the night. There was some dribbling between urination and at the end of urination. Under treatment this improved somewhat but not entirely. Eleven months after operation a cystoscopic examination was made, and this revealed several small pouchlike areas in the posterior urethra with several irregularities, giving one the impression that the musculature near the external sphincter had been injured.

On Jan 22, 1929, which was twenty-seven months after the operation, a cystogram was taken with the patient in both the horizontal and the erect postures. These revealed the outline of the bladder to be oval, after 200 cc of 35 per cent sodium iodide was injected. There was no leakage into the posterior urethra when the patient was in the horizontal position (fig 16). When he was erect

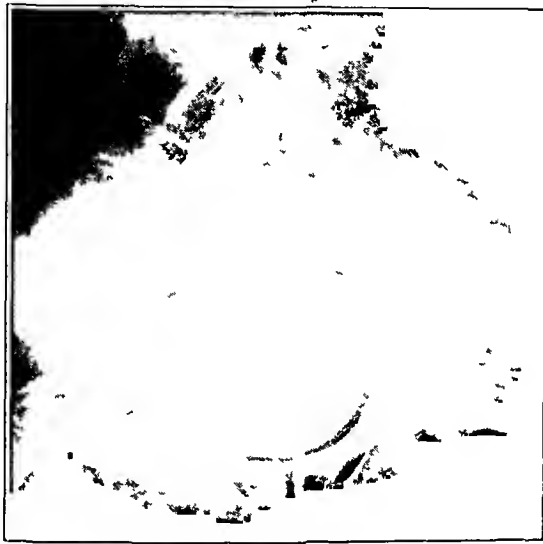


Fig 16—Cystogram taken with the patient in the horizontal position in a case of partial incontinence following perineal prostatectomy. The bladder outline appears normal with the point of bladder closure at the internal sphincter. No dye can be seen escaping through the internal or the external sphincter but in the upright position a few drops did leak past both sphincters.

it was observed that there was some leakage into the urethra and a few drops passed out through the external meatus. His condition, however, was improved. He could retain his urine at times as long as one and one-half hours without dribbling. Most of the dribbling was done in the afternoon. He could stop and start the stream in an excellent manner, but did have some dribbling between urination.

*Comment*—The resultant urinary incontinence in this case is of the partial type. Despite the fact that the patient is able to start and stop his stream voluntarily, he suffers from the inconvenience of wearing a small receptacle to catch the drippings when any sudden movement is made. There is a loss of from 1 to 3 ounces of urine during the day but none at night.

The persistence of diurnal dribbling implies that both vesical sphincters have been damaged to some extent. The derangement of the sphincters though relatively slight is permanent notwithstanding the ability of the patient to start and stop his stream. The damage to the external sphincter undoubtedly occurred when the urethrotomy incision for the insertion of the prostatic tractor was made high in the membranous urethra rather than close to the apex of the prostate. A contributory factor may be the faulty traction on the prostatic tractor in an upward direction which tends to split the external sphincter in the line of the urethrotomy incision. The injury to the internal sphincter most likely occurred when the prostatic adenoma was removed *en masse*. A more careful enucleation of the prostate from around the vesical orifice probably would have obviated some injury to the internal sphincter. However, we are inclined to believe that had we made the urethrotomy incision for the prostatic tractor at the apex of the prostate (as we do today) the external sphincter, the preservation of which is of paramount importance, would not have been injured and no incontinence would have resulted. In a careful dissection of the perineum in a perineal prostatectomy, the bulbous urethra and external sphincter should never be exposed.

CASE 3—J. A., aged 66, was admitted to the Sinai Hospital on June 20, 1928, in uremic coma. A history obtained from the patient on examination two years prior to admission was that he had urinary difficulty, such as urgency and diurnal and nocturnal frequency. A rectal and cystoscopic examination revealed a benign prostatic adenoma of the third degree. Owing to his condition of uremic coma, he was considered a very poor operative risk. Nevertheless, after fluids were forced and a retention catheter used, the patient's condition improved so much that on July 27 a perineal prostatectomy was performed, caudal anesthesia being used. Two lateral incisions were made in the prostatic capsule, and the lobes were removed separately. The median lobe was delivered into one of the lateral openings. The prostatic bridge of tissue was preserved, likewise the prostatic urethra, except for a small tear in the urethra which was made when the median lobe was delivered. The internal sphincter seemed undisturbed and was not unusually dilated, hence it was dilated with an instrument at the completion of the operation. The external sphincter was retracted up during the operation. Packs were placed in the capsule pressing against a urethral catheter which was inserted into the urethra, at the time of operation.

The catheter was removed on the fifteenth postoperative day, and the patient began voiding in a good stream, but he also dribbled between urination and at the end of urination. This was also noted when the patient would suddenly arise from a sitting posture. No nocturnal dribbling was present.

A cystogram (fig. 17), taken on Feb. 5, 1929, revealed a well outlined bladder with an imperfect closure at the internal sphincter. Some of the dye (35 per cent sodium iodide) leaked into the posterior urethra and out past the external meatus.

When the patient was last seen on April 4, 1929, the dribbling was still present.

*Comment*—This case illustrates the type of partial incontinence that may develop following a perineal prostatectomy. The causative factors of the incontinence are not quite clear, but undoubtedly both vesical sphincters were damaged during the operation.

The injury to the external sphincter was probably due to a faulty incision in the membranous urethra and may have been aggravated by the prolonged traction of the prostatic tractor. The damage to the internal sphincter is less easily explained since the prostatic adenoma was enucleated in separate portions, preserving the integrity of the posterior prostatic capsule and leaving the prostatic urethra intact except

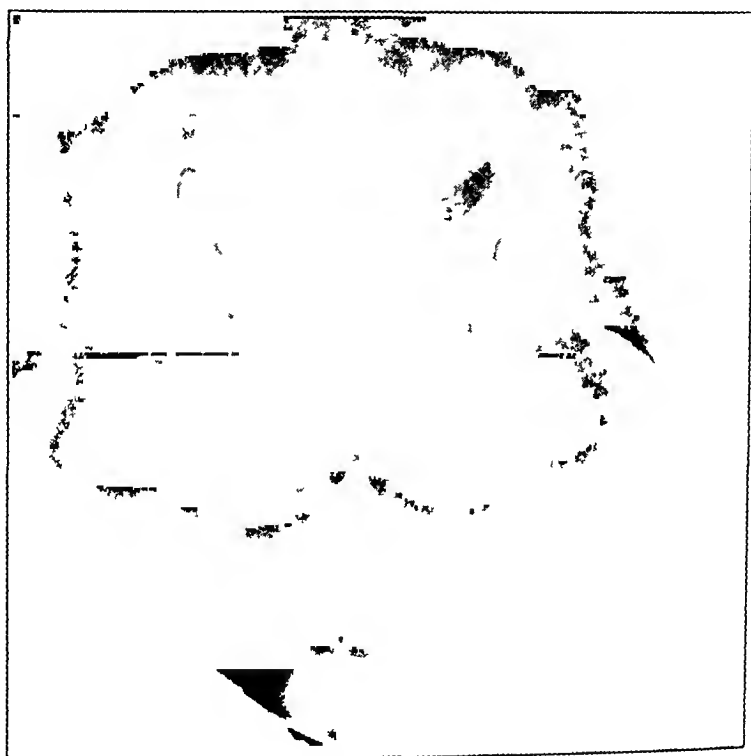


Fig 17—Cystogram in a case of partial incontinence following perineal prostatectomy. Imperfect bladder closure at the internal sphincter is noted. Some dye leaked into the posterior and anterior urethra.

for a small tear. At the completion of the operation, the internal sphincter appeared to be of good tone, and instrumental dilatation of this sphincter was performed as usual, which may have injured the sphincter. However it is conceivable that the internal sphincter was temporarily or permanently destroyed prior to operation by the dilatation accompanying the increased growth of the adenoma.

This patient also had a very large direct inguinal hernia on the right side occupying the entire scrotal sac. It was present before and after the operation and the patient refused operative treatment. While a large hernia may occasionally interfere with urination especially when

there is an accompanying herniation of the bladder, we are inclined to believe that the presence of the hernia did not influence the production of the persistence of the urinary incontinence, as cystographic and cystoscopic studies failed to reveal any bladder defect directly associated with the hernia

CASE 4—B L, aged 59, was admitted to Sinai Hospital on Sept 17, 1928, with symptoms of prostatic enlargement. Cystoscopic examination revealed a large intravesical bulging of the median lobe and a moderate intravesical and intra-urethral bulging of both lateral lobes. A diagnosis of benign prostatic adenoma of the second degree was made. The patient appeared to be a good surgical risk.

On October 5, perineal prostatectomy was performed with the patient under caudal anesthesia. An incision was made in the membranous urethra, close to the apex of the prostate for the insertion of the Young prostatic tractor. An inverted "U" incision was made in the capsule, and the prostate was removed en masse. The urethra was not preserved, but the prostatic capsule was. The prostate was of the adenomatous and fibrous type. At the completion of the operation, the internal sphincter appeared to be dilated. The external sphincter was retracted up with the transverse perineal muscles during the operation. A catheter was inserted into the bladder, and gauze packs were placed in the capsule against the catheter. The catheter was removed on the eighteenth day, and the patient began voiding, with some diurnal incontinence and terminal dribbling. As time went on, he began to get better control of urination. He could stop and start the stream, but he has never had perfect control. The patient was last seen on March 11, 1929, five months after the operation, and he had only partial control of the stream during the day. Dribbling was present between and at the end of urination. Dribbling also occurred while he was walking or sitting, and especially if he stood up suddenly. His stream was of good force.

A cystogram (fig 18), taken three months after operation, revealed partial closure of the bladder at the internal sphincter with some dye leaking into the posterior urethra. No dye escaped through the external sphincter which maintains bladder closure.

*Comment*—This case illustrates partial incontinence following perineal prostatectomy. The patient is able to pass urine in a good stream at fairly regular intervals. He is able to start the stream with ease, but there is some dribbling at the end of and between urination. Thus, at five months after operation, complete control of urination is lacking.

In this case, the incision in the urethra for the prostatic tractor was not made close to the apex of the prostate but rather high in the membranous urethra, with possible injury to the external sphincter. Misdirected traction of the prostate by the prostatic tractor may also have caused some injury to this sphincter. The prostatic enlargement was removed en masse taking with it the prostatic urethra and probably tearing some of the fibers of the internal sphincter. The injury to both sphincters could not have been complete, otherwise the patient would have had no control of urination.

CASE 5—W N, aged 76, was admitted to the Sinai Hospital on Nov 29 1918, with symptoms of prostatic enlargement. The usual examinations were made, including examination of the urine, blood, rectal, cystoscopic and roentgenographic studies. After a careful study, a diagnosis of benign prostatic adenoma of the third degree was made. The patient was considered a poor operative risk. The cystoscopic study, which is of importance in connection with this paper, revealed marked intra-urethral and intravesical bulging of the prostate. As the patient's general condition was very poor, the bladder was drained with a retention catheter for over three and a half months. After considerable difficulty and a long period of time, his general condition improved and a perineal prostatectomy was performed on March 18, 1919. Some of the details of the operation in this case were as follows: (a) two lateral incisions were made in the prostatic capsule through which one very large lateral lobe and the other very large lateral and moderate-sized median lobe combined were removed, and (b) the incision in the urethra for the tractor was made in the membranous portion above the apex of the prostate.

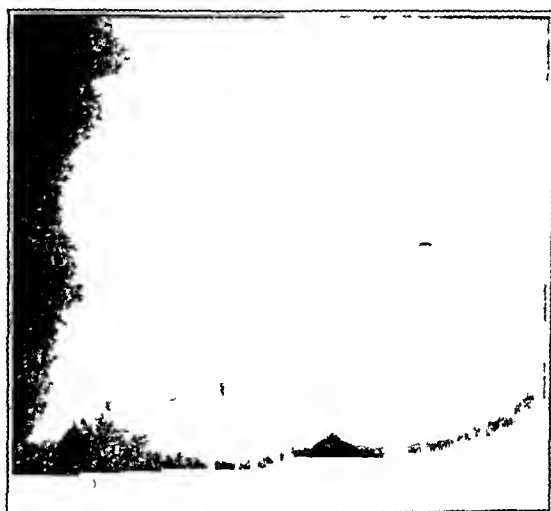


Fig 18—Cystogram in a case of partial incontinence following perineal prostatectomy. The bladder outline is normal. Partial bladder closure is noted at the internal sphincter with some dye leaking into the posterior urethra. No dye escaped through the external sphincter which maintains bladder closure.

At the completion of the operation, the internal sphincter seemed to be undisturbed and to have a fairly good tone. The urethra was partly injured during the removal of the median lobe. The external sphincter was thought likewise to be uninjured, but no particular observation of injury was made at the time. After closure of the perineal wound, which occurred on the nineteenth day, difficulty in urination was noted in that straining on urination and dribbling was present. Attempts were made to dilate the urethra, but these failed.

A diagnosis of urethral deformity or urethral stricture was made. On April 19, an external urethrotomy was performed. On May 2, the patient was discharged from the hospital voiding in a good stream but with slight dribbling at the end of and between urination.

After his discharge on May 2, he had diurnal and nocturnal incontinence and on Aug 29 1919, he was again admitted to the hospital for further observation. Cystoscopic examination at this time revealed a slight bulging at the right and

left anterolateral aspects of the vesical orifice, where two small lobulations were observed hanging down from the vesical orifice. There was marked relaxation of the posterior urethra. A perineal operation was performed on October 15, at which time repair of the external sphincter was attempted. A redundant membranous urethra was found, and plastic repair was performed for the formation of a new external sphincter. A catheter was inserted into the urethra. A stricture again resulted from this operation.

On Jan 19, 1920, he was again admitted to the hospital and dilatation was done with a filiform and followers. On one of these occasions, a filiform broke

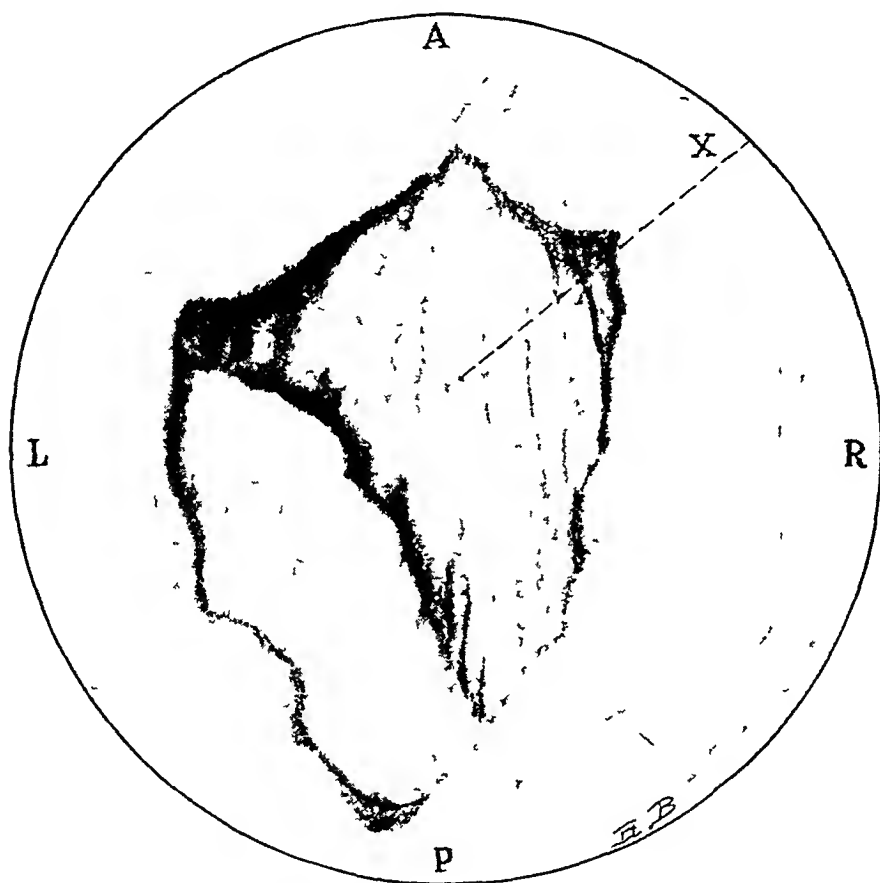


Fig 19—Relaxed and redundant posterior urethral walls with a ball of urethral tissue in a case of complete urinary incontinence following perineal prostatectomy in the authors' series. This patient also had a stricture in the posterior urethra about 2 cm from the vesical orifice which is not shown in the drawing. *X* indicates posterior wall of urethra. *A* indicates anterior, *P*, posterior, *R*, right, *L*, left.

off in the bladder, and an external urethrotomy was performed on February 18. The patient was discharged from the hospital on March 6. Complete urinary incontinence was present following these various operations. On March 1, 1921, he was again admitted for observation but was discharged on March 5. The last time the patient was heard from was six months after his last discharge from the hospital, at which time he still had incontinence.

CASE 6—B M, aged 59, was admitted to the Sinai Hospital with only mild symptoms of prostatic hypertrophy. Examination revealed an enlargement of the first degree in a man who was a good operative risk. Cystoscopic study revealed a few small calculi in his bladder. There was very slight bulging of the prostate laterally, but a moderate-sized median lobe was present.

A perineal prostatectomy was performed on Dec 16, 1927, with the patient under nitrous oxide anesthesia. A urinary obstruction developed after the perineal prostatectomy. The perineal fistula failed to close. At each act of urination all the urine drained through the perineal fistula, none passing through the urethral canal. The attempt to urinate caused the patient excruciating pain, owing to the inability of the urine to pass through the contracted internal sphincter. A stricture of the internal sphincter was diagnosed.

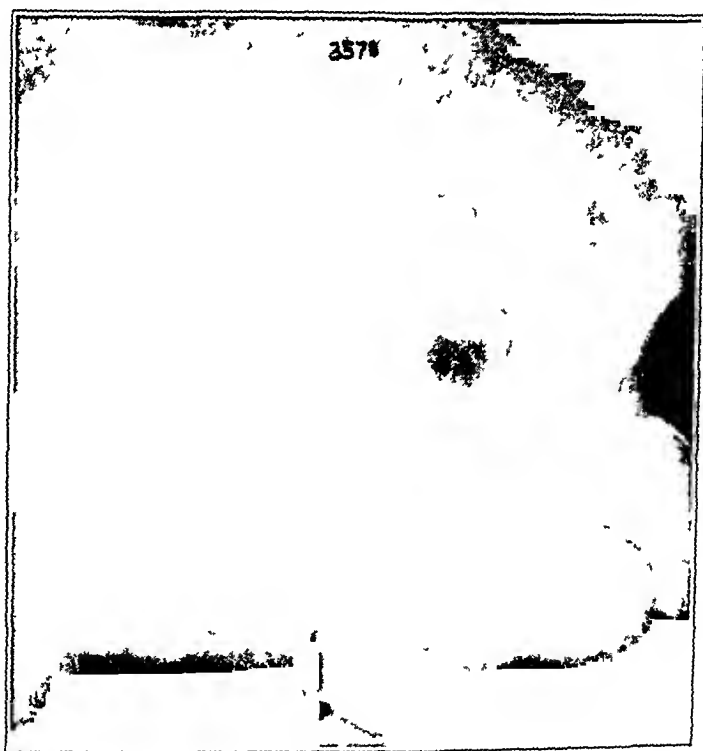


Fig 20—Cystogram in a case of complete incontinence following a perineal prostatectomy. The bladder outline is cone-shaped with cavity formation in the posterior urethra due to loss of function of the internal sphincter and to the presence of a stricture in the posterior urethra. Incompetency of the external sphincter is illustrated by the escape of dye into the anterior urethra.

On Jan 4, 1928 a plastic repair of the vesical neck was performed by the suprapubic route. At the operation, the internal orifice seemed somewhat dilated but in the region of the old prostatic urethra was found a flap of tissue which appeared to obstruct completely the outflow of urine (fig 19). Attempts to pass a sound beyond this obstruction through the urethra or retrograde from the bladder were unsuccessful. This was finally broken through. The urethra was then dilated and a catheter inserted. After the removal of the catheter urinary incontinence still existed, but urine came through the urethra with ease. The perineal wound was closed. Stricture of the posterior urethra developed shortly after operation, which necessitated another operation. A suprapubic cystotomy

with retrograde catheterization was performed on January 27, with little relief from the urinary difficulty

Urinary incontinence continued for one year. On Feb 12, 1929, plastic repair of the vesical orifice was attempted. No operation was performed on the membranous urethra at this time. The result was a failure as the urinary incontinence persisted. A bar was observed across the internal orifice. This was excised in the hope of relief.

When last seen, the patient had complete urinary incontinence. A further plastic operation is to be considered.

A cystogram (fig 20), taken after the prostatectomy, demonstrates a cone-shaped bladder with definite cavity formation up to the point of stricture in the posterior urethra. The dye has leaked past this strictured area into the anterior



Fig 21—Cystogram in a case of complete incontinence with the dye completely filling the anterior and posterior urethra, indicating total loss of function of the internal and external sphincters.

urethra. This cystogram illustrates the complete loss of function of both sphincters.

*Comment*—Cases 5 and 6 illustrate the occurrence of complete urinary incontinence following perineal prostatectomy. The etiologic factors and resulting anatomic defects appear to be the same in both cases.

Following the perineal prostatectomy, a stricture resulted which caused the incontinence. Despite repeated dilatations of the stricture and a secondary operation on it, the incontinence persisted.

In both cases the stricture occurred between the membranous urethra and the vesical orifice about 1 or 2 cm from the vesical orifice. The



vesical orifice was patent and dilated in each case but an obstruction to the passage of a sound was encountered just before the sound reached the vesical orifice. In addition there was an obstructing bar in one case (B M fig 19) which deflected the tip of the sound.

In both cases the urethrotomy incision for the insertion of the Young prostatic tractor was made high in the membranous urethra rather than close to the apex of the prostate. This procedure undoubtedly injures the external sphincter. The internal sphincter which is the sphincter most frequently injured in either a perineal or a suprapubic prostatectomy, was destroyed here by the tugging and trauma incidental to the removal of an adenomatous and fibrous gland intimately surrounding the internal sphincter.

Two cases of complete urinary incontinence came under our observation after perineal prostatectomy had been performed at another institution. Both patients had complete incontinence. In both cases cystoscopic study revealed a markedly dilated internal sphincter and relaxed external sphincter. In one case (fig 14) there was a redundant flap of the posterior urethra, and in the other case (fig 13) there was a redundancy and relaxation of the posterior urethral walls resulting in ledge formation in addition to a small lobulation of tissue on the posterior urethral wall. A cystogram in the latter case (fig 21) shows complete loss of bladder closure due to incompetent internal and external sphincters.

#### TREATMENT

Many operative procedures have been described for the treatment of postoperative urinary incontinence in the male. The methods vary from a plastic operation on both vesical sphincters through the combined suprapubic and perineal routes to the transplantation of a voluntary muscle (i. e., the levator ani rectus abdominalis pyramidalis etc.) about the neck of the bladder or urethra. We have attempted many of these methods in the treatment of postoperative urinary incontinence with varying degrees of success. A discussion of our experiences and results with these methods will be presented in a separate article to be published in the near future.

#### CONCLUSION

1 Urinary incontinence following suprapubic or perineal prostatectomy occurs more frequently than one would suspect after a thorough review of the literature.

2 In our series of 220 prostatectomies postoperative urinary incontinence of some degree occurred in 1 case (0.7 per cent) of 134 suprapubic and 5 cases (5.8 per cent) of 86 perineal prostatectomies.

3 Urinary incontinence occurs more frequently following perineal than suprapubic prostatectomy.

4 Urinary incontinence indicates a lack of complete control of the passage of urine through the urethra. The degree of incontinence may be complete or partial, depending on the degree of control of urination manifested.

5 Urinary incontinence may follow any suprapubic or perineal operation when both vesical sphincters are involved.

6 The occurrence of urinary incontinence following either type of prostatectomy is dependent on the destruction or derangement of both vesical sphincters.

7 The failure to preserve either the internal or external vesical sphincter will result in urinary incontinence.

8 In the hands of experienced surgeons, the probability of damaging either vesical sphincter is decidedly less during a perineal than during a suprapubic prostatectomy.

9 It appears that in the majority of cases the functioning sphincter following suprapubic and perineal prostatectomy is the external vesical sphincter, but in some cases of perineal prostatectomy the internal sphincter may also be preserved.

10 In our studies of prostatectomy we found that the etiologic factor in the production of urinary incontinence is more frequently injury during operation to the external sphincter than injury to the internal sphincter, as the internal sphincter may have been injured or destroyed prior to operation.

11 The type of hemostasis employed may influence the preservation or destruction of one or both sphincters.

12 Hemostasis in the suprapubic prostatectomy is essentially an intra-urethral compression of the enucleation cavity from above by means of gauze packs or hemostatic bags or metal cones. The same condition exists when a Davis bag is used for hemostasis in a perineal prostatectomy. Such a method tends to form a pouchlike deformity in the posterior urethra and to dilate further and possibly destroy the internal vesical sphincter.

13 Hemostasis when the perineal method is used is dependent on an intraprostatic compression maintained by packing the prostatic cavity (between the preserved urethral wall and the prostatic capsule) from below with gauze. In this manner, damage to the vesical sphincters is avoided.

14 Injury to the vesical sphincters can be avoided in a properly performed perineal prostatectomy (1) by retracting the external sphincter and transverse perineal muscles upward, (2) by making the urethrotomy incision for the introduction of the Young prostatic tractor below the external sphincter, preferably at or near the apex of the

prostate, (3) by an extra-urethral removal of the hypertrophied gland, leaving the internal sphincter and prostatic urethra intact, and (4) by exerting traction on the Young prostatic tractor in an upward and outward direction

15 The introduction of a catheter into the bladder through the urethra at the completion of a perineal prostatectomy facilitates the healing of an injured vesical sphincter and acts as a splint to preserve the continuity of the urethral walls

16 Various anatomic defects about the vesical neck and posterior urethra resulting from suprapubic and perineal prostatectomy may be associated with the loss of function of both vesical sphincters

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# ACTINOMYCOSIS OF THE THORAX<sup>4</sup>

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The cases of actinomycosis of the thorax have been divided into two groups—primary and secondary. Actinomycosis of the thorax is considered primary when the infection involves some organ or tissue within the thorax, primarily. Secondary actinomycosis of the thorax is a condition in which the organs or tissues of the thoracic cavity become involved secondarily to an actinomycotic lesion elsewhere in the body.

Clinically, Naussac<sup>1</sup> classified actinomycosis of the lung as (1) broncho-actinomycosis, (2) pneumo-actinomycosis and (3) pleuro-pneumo-actinomycosis. Choux<sup>2</sup> added a fourth group, thoracopulmonary actinomycosis, to designate the involvement of the thoracic wall.

In primary actinomycosis of the thorax, infection may take place by inhalation of the organism or by infection of the esophagus, from which the mediastinum, pleura and lung become involved. The lungs may be involved secondarily, by direct extension, by embolic or metastatic means, or in the manner in which primary actinomycosis is acquired, presumably as a result of the lesion in the body.

The manner in which the disease is acquired makes little difference in the ultimate outcome, as observed at necropsy. At postmortem examination of patients who have died of actinomycosis of the thorax, one frequently finds over the affected side one or more hard, indurated, bluish-red, boardlike swellings in which a draining sinus or several draining sinuses may be present. The most common sites of these actinomycotic abscesses are anteriorly, near the breast or in the axillary region, and posteriorly, near the angle of the scapula. If the tissue over one of these abscesses is incised, a fistulous tract which extends into the diseased pleura frequently may be found. When the ribs in such a region are exposed, occasionally elevation of the periosteum and some erosion of the rib will be found. When the thoracic cavity is opened

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<sup>4</sup> Submitted for publication, Nov. 25, 1929.

Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery, June, 1929.

1 Naussac Joseph. The Pathology, Symptomatology, and Differential Diagnosis of Pulmonary Actinomycosis, *Internat. Clin.* 3:1, 1921.

2 Choux, quoted by Naussac (footnote 1).

a thick fibrous pleura is encountered which is densely adherent to the thoracic wall by thick, fibrous bands, forming a meshwork in which small or large amounts of pus may be harbored. Numerous irregular canals may be found coursing through the thickened pleura. The canals may lead to an abscess or to a bronchus.

The lung may present two types of lesions. In one type the lung is large, edematous, heavy and leathery, this is known as the pneumonic type because on section, the appearance frequently is that of disseminated hepatization. Small, firm grayish-yellow nodules frequently are found scattered through the pneumonic area. If section is made through one of these nodules, it stands out above the surrounding tissue, and frequently a small amount of liquid material may escape from it. Careful examination of this material usually reveals the presence of a tiny, grayish-yellow granule, the sulphur granule. The sur-

TABLE 1—*Summary of Symptoms in Forty Cases of Primary Actinomycosis of the Thorax Recorded in the Literature*

Symptoms	Present	Not Recorded	Absent	Doubtful
Fever	34	1	1	4
Cough	36	1		3
Pain	38	2		
Expectoration	27	4	4	3
Hemoptysis*	3	5	17	5
External abscess	32	2	6	
Sinuses	23	8	9	
Loss of weight†	30	5	2	2
Involvement of ribs	10	10	9	11
Involvement of vertebrae	4			
Involvement of sternum	1			
Anemia	20	6	2	10

\* In ten cases the sputum was streaked with blood.

† One patient gained weight.

face of such a lung is usually irregular and rough as a result of broken adhesions. In the other type of lesion the lung is small, sclerotic and retracted toward the hilum. The surface of the lung is smooth.

The bronchial tree may show few changes. There is peribronchial fibrosis and, possibly slight thickening and edema of the walls. The lumen may be irregularly dilated, and at times a bronchus may be completely plugged with mucoid material.

Microscopically, the disease is characterized by marked hyperplasia of the interstitial connective tissue, large areas of granulation tissue, abscesses, integrity of the blood vessels and absence of giant cells.

#### PRIMARY LESIONS

This study is based on thirteen cases of primary actinomycosis of the thorax observed at the Mayo Clinic. The condition was also found in forty cases reported in the literature and the significant symptoms were tabulated (table 1) with a view of correlating the conditions in the two series.



*Age and Sex Incidence*—In the series of cases observed at the clinic eleven patients were males and two, females. The average age was 34 years. In the forty cases from the literature, twenty-seven of the patients were males and thirteen, females, a ratio of 2:1. The average age was 28 years in both sexes. The youngest patient suffering from the disease was a child, aged 2½ years, and the eldest, a man aged 65 years.

*Site of Election*—The side first affected was so predominantly the right in the present series of cases that I was surprised to find that several authors had stated that the left side was the one of election. This difference of opinion caused me to undertake an accurate study of the data from forty cases reported in the literature, with special reference to this point. Of the forty cases, the right lung was involved primarily in twenty, while the left lung was involved primarily in only fourteen, in five cases it was questionable whether the disease began in

TABLE 2—*Site of Involvement in Primary Lesions*

	Right Lung	Left Lung	Right and Left Lungs	Right or Left Lung?	Mediastinum	Not Given
Forty cases from literature	20	14		5		1
West	8	17	2			
Mayo Clinic	9	2		1	1	
Total	37	33	2	6	1	1

the right or in the left lung, and in one case the side involved was not mentioned. In West's<sup>3</sup> series, the lung primarily involved was the left in seventeen cases, the right in eight cases, and both lungs were involved primarily in two cases. In the series here reported, the right lung was involved primarily in nine cases, the left lung was involved primarily in two cases, the mediastinum in one case, and in one case, the side primarily involved was questionable (table 2).

From this review, it appears that the right lung is involved more frequently than the left. The site of election in the lung depends to some extent on the mode of infection. On account of the more vertical direction of the bronchus to the lower part of the right lung, inhaled foreign particles are more likely to go to this lobe. It is reasonable to conclude that the lower lobe of the right lung would be more frequently affected when actinomycosis is contracted by inhalation. If the lung becomes involved by means of the second source of infection the

<sup>3</sup> West, Samuel. Case of Primary Actinomycosis of the Pleura in a Child or Six, with a Table and Analysis of Recorded Cases of Primary Actinomycosis of the Lung and Pleura. *Tr. Path. Soc. London* 48: 17, 1897.

esophagus, then by virtue of its anatomic position one would expect the left lung to be the seat of the disease more frequently than the right

According to Cope,<sup>4</sup> the lower lobe is affected twice as frequently as the upper lobe. In West's series, the lower lobe was involved in thirteen cases, the upper lobe, in three cases, and the middle lobe in four cases

*Symptoms*—The patient dates the onset of his illness, in many instances, from the time a blow was received on the chest or shortly thereafter. Whether or not the impact is sufficient to create an injury or place of lowered resistance in the mucosa of the bronchial tubes or the esophagus is doubtful. However, such a history is sufficiently common to be noteworthy

The clinical symptoms of actinomycosis of the thorax may simulate those of two or three other diseases. The type of disease that the condition simulates, depends both on the mode of infection and on the extent to which the disease has progressed when the patient comes under observation

If the organism is inhaled, the first tissue to react is the bronchial mucosa. The reaction may be so limited that there will be no objective symptoms, and the organisms will pass immediately through the bronchial wall to involve the pulmonary parenchyma. On the other hand there may be rather diffuse stimulation of the mucous-forming cells of the bronchial tubes, giving rise to profuse expectoration, varying in character from almost pure mucous to fetid mucopurulent viscous sputum in which there are greenish-gray or yellowish-gray bodies. The symptoms are suggestive of simple catarrhal or mucous bronchitis when the sputum is mucoid, and bronchiectasis when the sputum is fetid. The typical sulphur granules may be found in the sputum at this time. Rarely, as in Canali's<sup>5</sup> case, the disease is confined to the bronchial tree. It may be said, therefore, that in the bronchial form the symptoms of actinomycosis are those of mucous bronchitis, occasionally accompanied by cough and usually associated with productive expectoration which may or may not be fetid, in which on careful, repeated examinations of the sputum, *Actinomyces* may be found

In some cases the organisms spread from the bronchus through the bronchial wall to involve the pulmonary tissue. In a few of these cases although involvement of the lung is widespread, there may be no symptoms indicative of organic trouble until late in the course of the disease

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<sup>4</sup> Cope V Z. A Clinical Study of Actinomycosis with Illustrative Cases. Brit J Surg 3 55 1915

<sup>5</sup> Canali quoted by Hektoen Ludwig. Actinomycosis of the Respiratory Tract. Internat Clin 2 97 1901

Frequently, however, the disease spreads rapidly along the bronchial tubes and bronchioles and produces, with the aid of secondary organisms bronchopneumonia. In this event, the patient will have fever, cough, pain, malaise, and other toxic symptoms, and the sputum may possibly be blood-tinged. The general and roentgenoscopic observations too, are those of bronchopneumonia. The disease runs the course of ordinary bronchopneumonia with the exception that the symptoms do not subside as quickly as would be expected in a case of simple pneumonia. After four or five weeks, the patient notes definite loss of strength and possibly some loss of weight, which, in conjunction with the history of cough and, at times, of blood-tinged sputum, lead the physician to suspect tuberculosis. In uncomplicated cases, repeated examinations of the sputum will be negative for bacilli of tuberculosis. At this stage a correct diagnosis is not often made and, consequently, the patient is treated for tuberculosis. In the course of time, the disease spreads peripherally to involve the pleura, and gives rise to the symptoms encountered in the pleuropulmonary form; the symptoms will be commented on under this heading.

In other cases, the symptoms may be solely those of an abscess, which may rupture into a bronchus and cause a quantity of pus to be expectorated. The associated fever and toxic symptoms are relieved thereby. On the other hand, the abscess may remain practically stationary, or may find a path to the pleura, eventually causing empyema. Roentgenoscopic examination of the thorax frequently will show the presence of an abscess.

In most cases, general examination shows the lesion in the lower lobe. Roentgenologic examination shows peribronchial infiltration with a rather marked degree of pulmonary fibrosis, if abscesses are present these frequently will be visible.

When the disease has progressed to involve the pleura, pain is usually an outstanding feature of the condition. Soon the patient will run a septic temperature, and will have night sweats and increasing dyspnea. Over the affected side, the respiratory excursion is decreased and dulness, or even flatness, and diminished breath sounds may be noted. A friction rub or râles may be present, depending on the type and extent of the lesion. A roentgenogram may show a thickened pleura or the accumulation of fluid. In the latter instance, a presumptive diagnosis of empyema usually is made. To confirm the diagnosis and determine the character of the lesion, thoracentesis frequently is done. Often the needle is inserted in many places before any fluid is found. If fluid is found instead of a large quantity, as in ordinary empyema, only from 2 to 5 cc. can be withdrawn into the syringe. This is rather typical of

actinomycosis and is due to the fact that the needle is inserted into one of the small pockets of pus. Sulphur granules often may be found in this fluid.

Once the disease has attacked the pleura it is only a matter of time before the process extends to involve the thoracic cage. The disease extends by direct growth and is especially prone to follow a puncture wound, such as is made in thoracentesis. A thick, leathery indurated process is present about the involved tissue, which eventually becomes red and tender, and fluctuates. At this time, the patient experiences pain, fever and toxic symptoms. When the abscess is drained the symptoms disappear, but a sinus is formed which drains indefinitely. The natural tendency of the disease is to spread to the surrounding tissue, and this tendency becomes much greater if the sinus heals and prevents free discharge of the fluid. In the course of time, a series of abscesses and as many sinuses form. If there is not ample drainage of these abscesses, the patient feels sick and weak and runs the typical course until drainage is reestablished.

If the disease is contracted by way of the esophagus, the mediastinum and pleura are involved first, and the symptoms will be similar to those described for a similar stage of the disease.

There are a few symptoms which occur with such regularity in the disease that it is worth while to comment on them at length. The data given are based on a study of the symptoms in this series of cases and the cases reviewed from the literature.

In practically all cases of actinomycosis of the thorax, fever develops during the course of the disease. Of the forty cases reviewed, there was a history of fever in thirty-four, in the other six, fever was not mentioned. In this series, nine patients had fever while under observation. The fever is probably due to invasion by a secondary organism, it is usually more pronounced in the evening, although it may occur in the morning. The temperature seldom runs higher than 101 F. If an abscess is present or if the invasion of secondary organisms is rapid, the temperature may go much higher. Fever due to abscess or empyema is of the septic type, and will disappear soon after adequate drainage is established. Fever due to a bronchopneumonic type of lesion will vary according to the progress of the disease.

Expectoration is present in from 60 to 70 per cent of the cases and varies considerably in amount. It is often streaked with blood, probably on account of suppuration and rupture of peribronchial granulomas. Often it is fetid, reminding one of the sputum in bronchiectasis. Occasionally it is viscous and on standing separates into two layers, the upper layer is mucous, the lower layer is viscous and is composed

of a yellow sediment in which the elements of *Actinomyces* may be found

Hemoptysis is relatively rare. Of forty cases in the literature, in only two had there been definite hemorrhage, in one of these, about 125 cc of blood had been expectorated. In a third case there had been considerable blood in the sputum for four days. All of these patients died. In the present series there had been sudden hemorrhage from the lung in one case, but subsequent recovery was remarkable. The reason hemorrhage is so rare in actinomycosis of the lung, as Naussac pointed out, is the almost total lack of erosion of the wall of the vessel even "in an abscess undergoing purulent melting." This integrity of the blood vessels is characteristic of actinomycosis and distinguishes it from tuberculosis. As noted, the sputum often is streaked with blood, possibly owing to rupture of peribronchial granulomas.

During the course of the disease, practically every patient suffers pain. The character of the pain may vary greatly. It may be an intermittent "sticking" type felt through the thorax, which is hardly severe enough for the patient to note. In some cases, it may be a sense of constriction through the thorax. When the pleura is involved the pain is much more severe and may become incapacitating. The character of the pain frequently changes after a few days from a sharp respiratory type to dull, constant pain. Occasionally, the disease spreads to involve the vertebral column and the anterior nerve roots, and causes root pain. Complications, such as rupture of an abscess from the pleural cavity into the peritoneal cavity, producing severe, cramplike pains and collapse, must be kept in mind. The psoas muscle is involved in some cases, frequently, this gives rise to painful contracture which necessitates the application of Buck's extension for relief.

Cough is a symptom in 90 per cent of the cases, although it may not be bothersome. If the disease starts as apparent bronchitis or bronchopneumonia, cough occurs early and may subside as the disease progresses. In other cases, it does not appear until late. Usually, the cough is productive, less frequently, it is a nonproductive, hacking cough, and occasionally it is paroxysmal.

The sense of weakness may be the first and chief complaint. Late in the course of the disease, it is a constant complaint. Dyspnea is experienced in about 40 per cent of the cases, it is present when the lung is sufficiently involved to embarrass respiration, and is more commonly present in the sclerotic type of lesion of the lung. Although this symptom may occur early in the course of the disease, it is usually late. The early manifestation of involvement of the pleura is serous

pleuritis, which becomes purulent pleuritis or empyema as a result of the invasion of secondary organisms. An actinomycotic abscess may perforate into the pleura and produce empyema. The empyema pocket may be large, but more often it is small, because of interlacing fibrous adhesions. Anemia is noticeable rather late in the disease in from 65 to 70 per cent of the cases. In this series, the average percentage of hemoglobin was 67, but in some cases the percentage of hemoglobin was as low as 29, and transfusion had to be given. Marked loss of weight is the rule. In this series, the average loss of weight was 34 pounds (15.4 Kg). In an occasional case, weight will be gained for a time at least. Night sweats are noted only if the condition is definitely septic or the patient is markedly debilitated. Clubbed fingers were evident in only one case, and in this case empyema had developed. In all probability, such a condition occurs only in the presence of associated purulent pulmonary complications. Because of the close proximity of the diseased pleura to the thoracic wall, the latter becomes involved in from 80 to 90 per cent of the cases. A fistulous opening from the pleural cavity to the soft tissue of the thorax frequently is found.

In the region of the abscesses there may be definite erosion of the ribs. The ribs were definitely involved in 25 per cent of the cases noted in the literature, whereas the vertebrae were involved in 10 per cent. Occasionally, actinomycotic osteomyelitis may be present. In one of the cases there was osteomyelitis of the sternum.

*Diagnosis*—The diagnosis depends on the finding of *Actinomyces* in the sputum or in the pus of an abscess or sinus or on demonstration of the actinomycotic lesion in a histologic specimen. One may be aided in making a presumptive diagnosis of actinomycosis by (1) the character of the sputum, (2) persistent symptoms of bronchopneumonia, (3) induration and formation of abscesses and sinuses in the soft tissue of the thorax, and (4) examination by roentgen ray.

*Differential Diagnosis*—The long duration of symptoms practically rules out simple pneumonia. Tuberculosis is perhaps the most likely presumptive diagnosis. Against this diagnosis are the following facts. The lesion is basal, repeated examinations of the sputum are negative for bacilli of tuberculosis, and the roentgenologic data are not typical of tuberculosis. The correct diagnosis is made solely on the presence of *Actinomyces* in the sputum. At this stage, this organism is found with relative infrequency.

*Treatment*—The patient should be put on a full diet and be given plenty of sunshine and fresh air. Special forms of treatment also have been found to be helpful.

The use of potassium iodide in the treatment for actinomycosis is empiric. Its action, as stated by Lieblein,<sup>6</sup> is to bring about solution of the cellular infiltrative process about the abscess and the consequent discharge of *Actinomyces*, in imitation of nature's own method of healing. Several cases have been reported in which the organisms were found in great numbers in the sputum prior to the use of the drug but disappeared rapidly under its use. A short time later, at necropsy, *Actinomyces* could be demonstrated only by the most diligent search, although the pathologic structural changes were present in abundance. Progressively increasing doses of saturated solution of potassium iodide are given three times a day until the patient is taking 600 minims (36.96 cc) daily, or until the point of tolerance is reached. Chittv<sup>7</sup> prefers the use of tincture of iodine to potassium iodide. He gives from 6 to 10 minims (0.37 to 0.61 cc) of the tincture of iodine in milk three or four times daily, and his results are rather striking. The iodine apparently is readily absorbed when given in this manner. The intravenous use of sodium iodide has no advantage over the oral administration of potassium iodide.

Treatment by roentgen ray and radium has given excellent results in certain cases. The symptoms have been attenuated, and life apparently has been prolonged in many cases, in some cases on record the disease apparently has been arrested by the use of roentgen ray and radium. The success of such treatment depends necessarily on the stage to which the disease has progressed and on the site of the lesion. Surgical procedures are indicated only to establish and maintain ample drainage of abscesses and of empyema pockets.

*Course*—In the majority of the cases the course is progressively downward, it is characterized by increasing weakness, dyspnea, cough, pain, loss of weight and increasing anemia. The outcome is usually fatal, and death results from the debilitating effects of the disease or from secondary infection. There are a few chronic cases, however, in which the symptoms extend over a period of years. In such cases the patients usually feel well if there is ample drainage of the abscesses or empyema pockets. If an abscess forms, or if there is insufficient drainage the patient experiences toxic symptoms of a varying degree of severity. If there is ample drainage of the abscess, the patient regains a fair state of health. In other cases, the disease apparently has been arrested. The average duration of symptoms, from probable onset to death in the twenty-seven cases recorded in the literature, was

6 Lieblein, quoted by Erving, W. G. *Actinomycosis Hominis in America* with Report of Six Cases, *Bull. Johns Hopkins Hosp.* **13**: 261, 1902.

7 Chittv, Hubert. *Actinomycosis Successfully Treated by Iodine in Milk*. *Brit. M. J.* **1**: 418, 1926.

eight months. The vast difference in duration of symptoms between the series reviewed in the literature and the series seen at the clinic, probably is due to one or both of two factors. The more important factor of the two, perhaps, is the advanced stage of the disease when the patients whose cases are recorded in the literature presented themselves for treatment. The second factor is concerned with the treatment for the disease. Many of the cases recorded in the literature occurred before the day of treatment by roentgen ray. The average duration of symptoms from the probable date of onset of the disease to death,

TABLE 3—*Summary of Symptoms in Thirteen Cases of Primary Actinomycosis of the Thorax Seen at the Mayo Clinic*

Symptoms	Present	Not Recorded	Absent	Average
Fever	9		1	
Cough	9	3	1	
Night sweats	5	6	2	
Pleurisy	10	1	2	
Weakness	11	2		
Pain	11	2		
Expectoration	6	6	1	
Loss of weight, pounds				34
Hemoglobin, per cent				67
Sinuses	10	1	2	
Empyema	3	9	1	
Blood pressure				123
Systolic				77
Diastolic				

TABLE 4—*Result of Treatment and Duration of Symptoms in Forty Cases of Primary Actinomycosis of the Thorax Recorded in the Literature*

Result	Cases	Per Cent	Duration of Symptoms Months	Duration of Symptoms Not Given, Cases
Dead	27	67.5	8	5
No improvement	6	15.0	14	1
Improved	4	10.0	24	
Arrested	1	2.5	2	
Not given	2	5.0		

c

in the series observed at the clinic, was twenty-nine months. The average duration of symptoms between registration at the clinic and establishment of the diagnosis was fifteen months.

*Results of Treatment*—Of the thirteen cases in the present series, death has occurred in six (47 per cent). In two cases there has not been improvement, in one case there has been apparent improvement, and in another case the condition seems to have been completely arrested. In three cases, follow-up data have not been obtained (table 3).

If the results obtained in this series are compared with the results obtained in the cases recorded in the literature (table 4), one finds in



the latter that in the forty cases, twenty-seven patients (67 per cent) died. In six cases improvement did not occur, temporary improvement was noted in five, and there were no follow-up data in two cases. One patient was reported as well, but the duration of the "arrested stage" in this case was only two months, a period far too short to pronounce a patient "well" in this disease.

I believe that a combination treatment, consisting of the administration to tolerance of a saturated solution of potassium iodide, together with treatment by roentgen ray and radium and ample drainage, when indicated, has definitely prolonged the life of the patient and attenuated the symptoms, particularly in cases in which treatment was administered early in the course of the disease.

*Prognosis*—The disease is almost always eventually fatal. In a report of eighty-seven cases of actinomycosis seen in Norway, Harbitz and Grondahl<sup>8</sup> stated that the thorax was involved in 23 per cent. All of these patients died. Other authors have stated that the mortality rate is from 60 to 75 per cent. Such an estimate is based on the known death rate in a series and does not take into consideration the probable mortality in those cases listed as unimproved, improved and so forth. The duration of symptoms from onset to death is from eighteen months to two years. In an occasional case, to the contrary, the course will be markedly rapid, and death will occur in from one to five months. The symptoms in a few cases will be drawn out over a period of from six to eight years. In rare instances, there seems to be spontaneous and final arrest of the process.

#### SECONDARY LESIONS

This study is based on data concerning sixteen patients suffering from actinomycosis with secondary involvement of the thorax. In this series, the primary lesion was in the abdomen in 94 per cent of the cases. In one case the primary lesion was on the tibia, many years later, an esophagobronchial fistula developed with secondary pulmonary involvement. The thorax becomes involved secondarily by direct extension, by dissemination through the blood stream or by the introduction of the organism into the mouth.

The right side of the thorax was affected in ten cases (63 per cent, table 6). Involvement was of the left side in two cases, of the right or left side in one case and of both right and left sides in three cases. The predominance of the condition in the right side is readily explained by the fact that the majority of the primary lesions are in the right

<sup>8</sup> Harbitz, Frances, and Grondahl, N. B. Actinomycosis in Norway. Studies in the Etiology, Modes of Infection and Treatment, *Am J M Sc* 142: 786, 1911.

side of the abdomen, and that the thorax becomes involved secondarily by direct extension in a high percentage of cases. If the disease is carried to the lungs by the blood stream, either or both lungs may be affected.

The lesions encountered in secondary actinomycosis of the thorax are similar to those in primary actinomycosis of the thorax. The symptoms and the course of the disease are similar (tables 5 and 6). With secondary thoracic involvement, the patient complains of greater weakness, and night sweats are more troublesome. Anemia is more

TABLE 5—*The Primary Site of Actinomycosis in Sixteen Cases Involving the Thorax, Secondarily*

Primary Site of Lesion	Cases	Per Cent
Ileocecal region or appendix	10	62.5
Appendix or sigmoid	1	6.3
Tonsil or appendix	1	6.3
Gallbladder or appendix	1	6.3
Abdominal wall	1	6.3
Tibia or larynx	1	6.3
Right upper part of abdomen	1	6.3

TABLE 6—*Summary of Symptoms in Sixteen Cases of Actinomycosis with Secondary Involvement of the Thorax*

Symptoms	Present	Not Recorded	Absent	Average
Fever	9	4	3	
Cough	6	6	4	
Night sweats	11	3	2	
Pleurisy	11	3	2	
Weakness	10	5	1	
Pain	14	2		
Expectoration	7	8	1	
Sinus	13		3	
Empyema	3	4	9	
Hemoglobin, per cent				51.5
Loss of weight, pounds				34.5

pronounced in the secondary type, whereas the loss in weight is about the same in both types.

When the thorax becomes involved secondarily, the disease usually has progressed beyond the point where one could hope to arrest it. The symptoms may be attenuated and life prolonged by following the line of treatment outlined for primary actinomycosis of the thorax. In sixteen cases, nine patients (56 per cent) died. Three patients were improved. Follow-up data were not obtainable in four cases.

The average duration of symptoms from the date of probable onset of the disease to death was three years. The duration of symptoms in one case was extremely long. If this case were not included in computing the duration of symptoms, the average duration of symptoms would be eighteen months (figs 1 to 4).

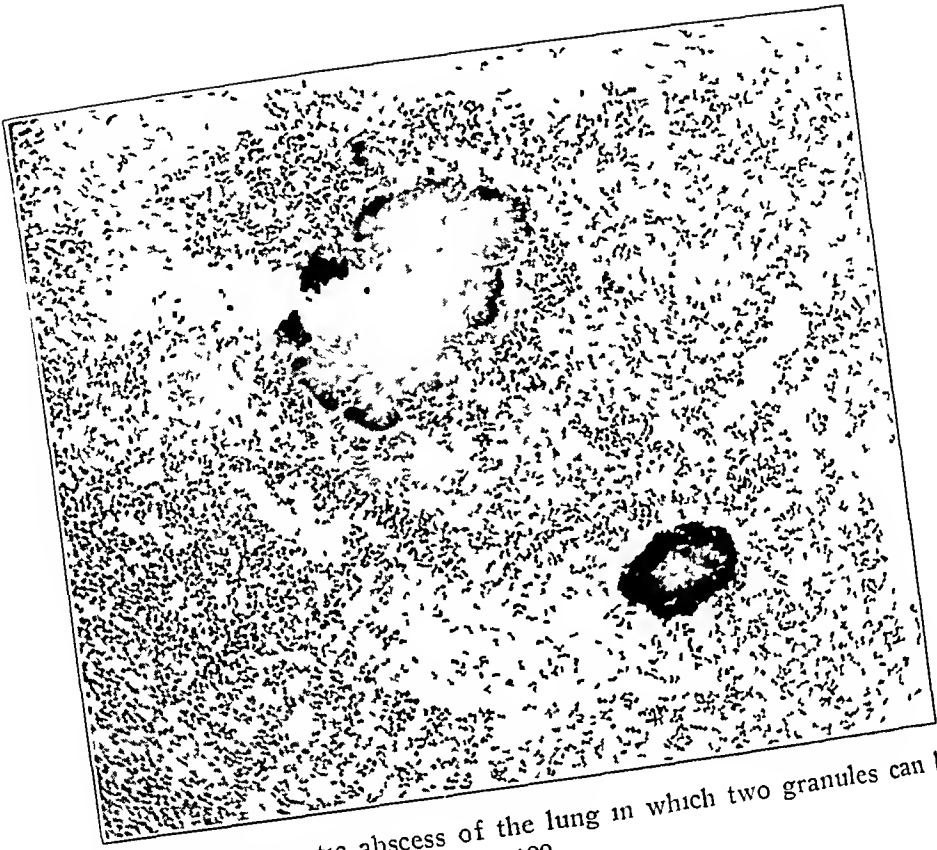


Fig 1—Actinomycotic abscess of the lung in which two granules can be seen  
is shown, hematoxylin and eosin,  $\times 100$

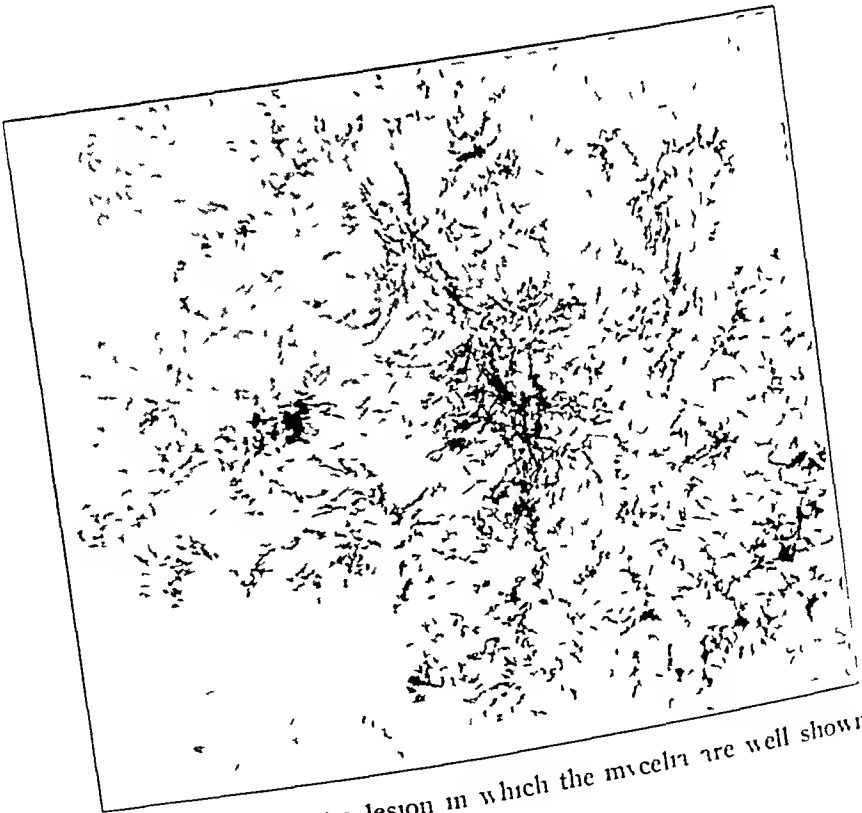


Fig 2—An actinomycotic lesion in which the mycelia are well shown  $\times 170$

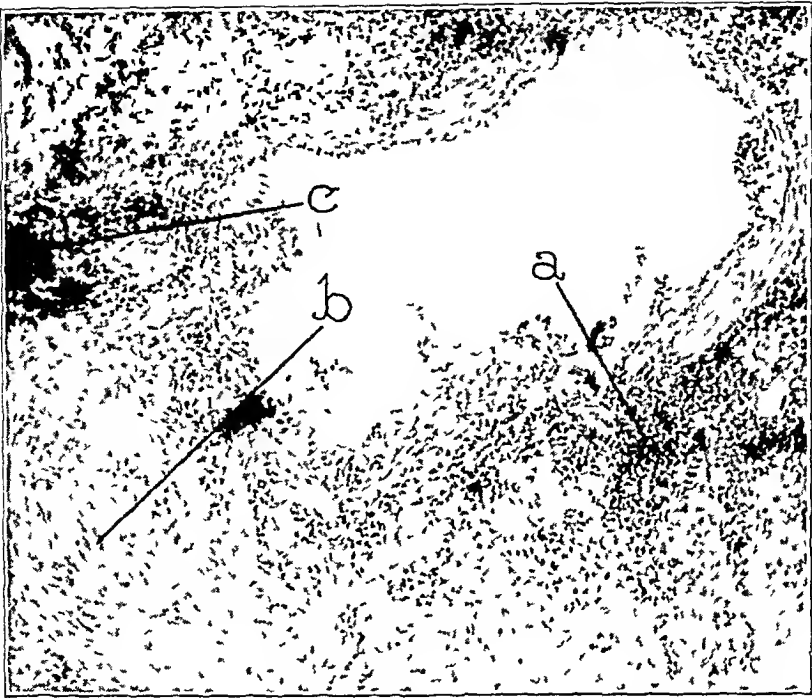


Fig 3—A large blood vessel is surrounded by granulation tissue of an actinomycotic lesion of the lung, *a*, an abscess just lateral to the vessel is seen to involve its wall, *b*, whorls in granulation tissue, and *c*, lung is laden with carbon pigment, hematoxylin and eosin,  $\times 75$

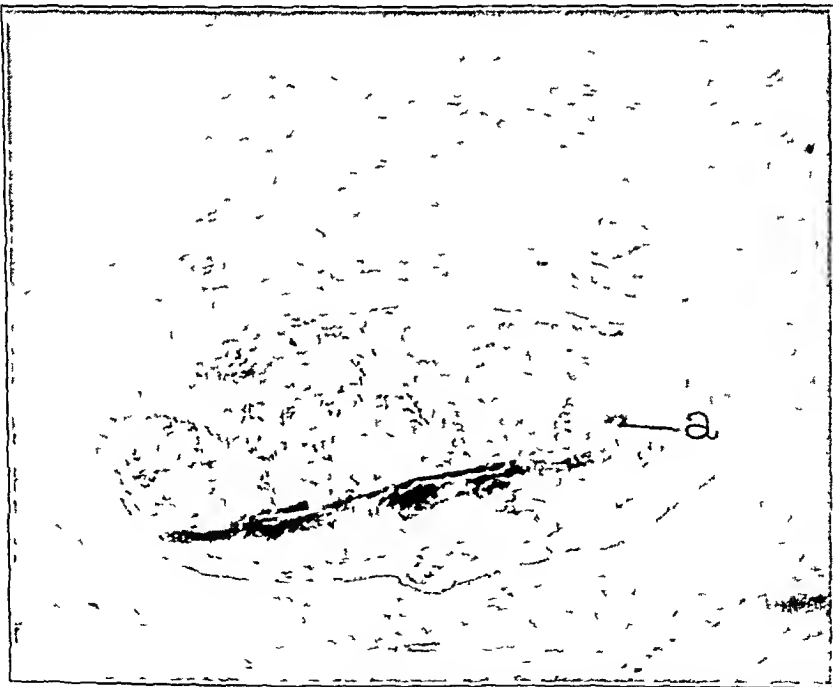


Fig 4—A bronchus is filled with detritus of an actinomycotic lesion, *a*, actinomycetes hematoxylin and eosin,  $\times 75$

## SUMMARY

The symptoms of actinomycosis of the thorax may simulate those of bronchitis, bronchopneumonia, pulmonary abscess and pulmonary tuberculosis. The more common symptoms are fever, cough, sputum, pain, weakness, loss of weight, dyspnea, anemia and external abscesses.

The diagnosis of actinomycosis is made (1) by demonstrating the sulphur granule in the sputum, in empyema fluid or in the pus from an abscess, or (2) by demonstrating the actinomycotic lesion in a histologic specimen.

Treatment should be directed at improving the general health, the administration to tolerance of potassium iodide, the drainage of abscesses and empyema pockets, and the proper use of roentgen ray and radium.

The disease is fatal in from 60 to 70 per cent of the cases.

# INTRACRANIAL CALCIFICATION

WITH PARTICULAR REFERENCE TO THAT OCCURRING IN  
THE GLIOMAS \*

CYRIL B. COURVILLE, M.D.

AND

LEO J. ADELSTEIN, M.D.

LOS ANGELES

Areas of intracranial calcification are not uncommonly seen in roentgenograms of the skull, associated with conditions of both a physiologic and a pathologic nature. This is particularly true since the Bucky diaphragm has made it possible to demonstrate the minute details of the skull and any calcareous material of any magnitude within it. The question will consequently arise as to the nature of the associated lesion, particularly if the roentgenograms were taken with the hope of establishing the diagnosis of an obscure disease of the brain. It is our purpose in this study to note first the pathologic possibilities and then to discuss more in detail calcification within intracranial tumors, particularly the gliomas. This is of special importance to the surgeon, for a calcified tumor not only gives positive testimony as to its situation, but also encourages him to believe that it has benign tendencies.

## CALCIFICATION IN REGRESSIVE AND DEGENERATIVE PROCESSES

Calcification in the pineal body may be seen in the majority of roentgenograms of the skull of adults. Several years ago, Schuller<sup>1</sup> called attention to the dislocation of calcified pineal bodies from the midline in intracranial tumors, a fact reaffirmed more recently by Naffziger<sup>2</sup>. Vastine and Kinney,<sup>3</sup> in reviewing the roentgenograms in 616 cases of suspected intracranial tumor in which calcification of the pineal bodies was observed, made a note of its position in relation to the anteroposterior and vertical diameters of the skull as measured on the lateral plate. They found that its dislocation beyond certain limits is a valuable aid in the localization of intracranial lesions. Calcification is

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\* Submitted for publication March 14, 1930

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1 Schuller, Arthur. Roentgen Diagnosis of Diseases of the Head, translation by Stocking, St. Louis, C. V. Mosby Company, 1918, p. 156.

2 Naffziger, H. C. A Method for the Localization of Brain Tumors. The Pineal Shift. Surg. Gynec. Obst. **40**: 481 (April) 1925.

3 Vastine, J. H. and Kinney, K. K. The Pineal Shadow as an Aid in the Localization of Brain Tumors, Am. J. Roentgenol. **17**: 320 (March) 1927.

also occasionally seen in the choroid plexuses of the lateral ventricles, appearing as flocculent masses on one or both sides as oriented in stereoroentgenograms. While its significance is not clear, calcification in these structures may be of an irritative or chronic inflammatory nature.

At times, calcification in sclerosed vessels forming the circle of Willis may be observed in the roentgenogram.<sup>4</sup> Chronic inflammatory conditions are probably responsible for the presence of the calcification and ossification in the arachnoid and dura mater.<sup>5</sup> True bone formation of any size is found most frequently in the dura, especially in its reduplication, the falx cerebri.<sup>6</sup> Calcium is occasionally deposited in traumatic scars of the brain, softenings of the brain and old cerebral hemorrhages. It may also be found in the form of small granules in chronic degenerative and inflammatory processes, such as Parkinson's disease,<sup>7</sup> encephalitis,<sup>8</sup> malaria,<sup>9</sup> and in toxic conditions, such as carbon monoxide poisoning.<sup>10</sup> Macewen<sup>11</sup> found calcium in the walls of chronic abscesses of the brain.

It may also occur in that borderline heterotropia, lying between the congenital malformations on one hand and true tumors on the other—tuberous sclerosis. In this condition calcium is commonly found in the walls of the small blood vessels<sup>12</sup> and may be responsible for the convulsions characteristic of the lesion. The surgical removal of tissue

4 Holmes, G. W. and Ruggles, H. E. *Roentgen Interpretation*, ed. 3, Philadelphia, Lea & Febiger, 1926, p. 117.

5 Cushing, Harvey, and Weed, L. H. *Studies on the Cerebro-Spinal Fluid and Its Pathway*. IX. Calcareous and Osseous Deposits in the Arachnoidea. *Bull. Johns Hopkins Hosp.* **26**: 367 (Nov.) 1915. Halstead, A. E., and Christopher F. *Calcification and Ossifications of the Meninges*, *Arch. Surg.* **6**: 847 (May) 1923.

6 Dr. Ray A. Carter, roentgenologist to this hospital, called our attention to the occurrence of calcification in the attachments of the tentorium to the clinoids. In the roentgenogram, small masses of calcareous material appeared as hornlike projections of the posterior clinoids.

7 McAlpine, Douglas. *The Pathology of the Parkinsonian Syndrome Following Encephalitis Lethargica*, with a Note on the Occurrence of Calcification in This Disease, *Brain* **46**: 255, 1923.

8 Calcification in encephalitis has been observed by others (Spatz *Ztschr. f. d. ges. Neurol. u. Psychiat.* **77**: 261, 1922), but the essential process is probably the same in this as in other chronic degenerative or toxic conditions. The calcareous material seems to be deposited chiefly in the walls of the blood vessels.

9 Seifarth. *Deutsches Arch. f. klin. Med.*, 1921, vol. 134, quoted by Kaufmann [footnote 12 p. 1919].

10 Eaves, E. C. *A Contribution to the Study of Deposits Containing Calcium and Iron in the Brain*, *Brain* **49**: 307, 1926.

11 Macewen, William. *Pyogenic Infective Diseases of the Brain and Spinal Cord*, New York: The Macmillan Company, 1893, p. 109.

12 Kaufmann, Edward. *Pathology for Students and Practitioners*, translated by Reimann. Philadelphia, P. Blakiston's Son & Company, 1929, vol. 3, p. 144.

in which calcification was found in blood vessels was recently reported by Geyelin and Penfield,<sup>13</sup> the lesion was probably of this type

#### CALCIFICATION IN INTRACRANIAL TUMORS

Calcareous deposits have been known to occur in almost every variety of primary new-growth that compromises the intracranial space. It has been observed in gummas and tuberculomas of the brain, although we have not encountered it in any such lesions coming under our direct observation. It is also rarely found in the walls of parasitic cysts, where it assumes a more or less crescentic shape conforming to the walls of the cyst. Calcification in these conditions is indicative of a quiescent process.

The presence of flocculent shadows in or above the sella in roentgenograms of cysts arising from the remains of the craniopharyngeal canal is of particular interest. Luger,<sup>14</sup> in reviewing the literature, indicated that calcification in this type of tumor has been noted for many years both in the roentgenogram and in the gross specimen. He mentioned the cases of Algyogyis, Spinzels, Engelman, Erdheim and Walker, and the possible cases of Aschoff, Benda, Bregman and Steinhaus, and Boryces and Radla. Heuer and Dandy<sup>15</sup> found one case of this type of tumor in the roentgenographic studies of a hundred consecutive cases of tumor of the brain. Recently, in a more comprehensive report, McKenzie and Sosman<sup>16</sup> considered in greater detail the type and distribution of the calcareous particles in the walls of the cysts. They found that it occurred in 70 per cent of the cases, its appearance in the roentgenogram constituting thereby a valuable diagnostic sign.

While aneurysms of the larger cerebral vessels have been recognized for almost two hundred years, until recently little or no attention has been paid to calcification occurring in their walls. Schuller<sup>1</sup> seems to have been the first to call attention to the characteristic crescent-shaped plaques in lateral roentgenograms of the skull. Heuer and Dandy<sup>15</sup> reported a typical case in their series. Sosman and Vogt<sup>17</sup> in reporting

13 Geyelin H. R., and Penfield, Wilder. Cerebral Calcification Epilepsy, Endarteritis Calcificans Cerebri, Arch. Neurol. & Psychiat. **21** 1020 (May) 1929.

14 Luger Alfred. Zur Kenntnis der im Röntgenbild sichtbaren Hirntumoren mit besonderer Berücksichtigung der Hypophysengangesgeschwülste, Fortschr. a. d. Geb. d. Röntgenstrahlen **24** 605, 1914.

15 Heuer, G. J. and Dandy, W. E. Roentgenography in the Localization of Brain Tumors, Based upon a Series of One Hundred Consecutive Cases, Bull. Johns Hopkins Hosp. **26** 311 (Nov.) 1916. In this contribution, the authors note the early roentgenographic demonstration of calcification in intracranial lesions. Among others are mentioned calcification in a gumma (Lichtheim), cysticercus cyst (Stieda), abscess of the brain (Strater), pineal tumor (Grunmach) and tumors of the brain (probably gliomas) by Schuller and Klineberger.

16 McKenzie K. G. and Sosman M. C. The Roentgenological Diagnosis of Craniopharyngeal Pouch Tumors. Am. J. Roentgenol. **11** 171 (Feb.) 1924.

17 Sosman M. C. and Vogt E. C. Aneurysms of the Internal Carotid Artery and the Circle of Willis. Am. J. Roentgenol. **15** 122 (Feb.) 1926.



a series of ten cases verified at autopsy, considered two that gave roentgenographic evidence of the plaques. In a second series of ten unverified cases, six showed the typical semilunar plaques in their walls. Such observations are indicative of the larger aneurysms, as the smaller forms give no roentgenographic evidence of their presence, except for a minor degree of erosion of the clinoids.

Tumors that had their origin from the meninges were probably the first to be demonstrated roentgenographically. The historical cases of Obici and Bollici,<sup>18</sup> and of Mills and Pfahler<sup>19</sup> were undoubtedly of the type known as "endotheliomas" and more recently as meningiomas or meningeal fibroblastomas. There are several roentgenographic characteristics of this form of intracranial tumor, as has been emphasized by Sosman and Putnam,<sup>20</sup> but the one which concerns us in this connection is that of calcification within the tumor itself. This is rather rare as far as the larger masses visible roentgenographically are concerned, but not infrequently small granules of calcareous material are encountered in the gross specimen. These are probably too small to be seen in the roentgenogram, their shadow being "burned out" in the exposure necessary to get clear detail in the skull.

Mention has been made in the literature of shadows in the sella observed in roentgenograms of the skull in cases in which a pituitary tumor was demonstrated at necropsy.<sup>21</sup> That true calcifications may occur in the pituitary adenomas has been known for some time, but verification for some reason has been delayed until recently. Deery,<sup>22</sup> in a series of 285 pituitary adenomas studied at Cushing's clinic, found 19 in which shadows of calcium could be seen in the roentgenogram. The calcareous material of one of these tumors was subsequently demonstrated histologically.

Calcium has been found in some of the cases of angiomas of the cerebral vessels. In their monograph, Cushing and Bailey<sup>23</sup> collected

18 Obici and Bollici. Applicazione dei raggi "x" alla diagnosi di sede dei corpi estranei della testa e dei tumori intracranici, *Riv di patol nerv* **11** 433, 1897, quoted by Sosman and Putnam (footnote 20).

19 Mills, C. K., and Pfahler, G. E. Tumor of the Brain Localized Clinically and by the Roentgen Rays, *Philadelphia M J* **9** 268 (Feb 8) 1902. Mills, C. K., Pfahler, G. E., and Deaver, J. B. An Additional Case of Tumor of the Brain Localized Clinically and by the Roentgen Rays, *Philadelphia M J* **10** 439 (Sept 27) 1902.

20 Sosman, M. C., and Putnam, T. J. Roentgenological Aspects of Brain Tumors. Meningiomas, *Am J Roentgenol* **13** 1 (Jan) 1925.

21 Marques and Peyron. *Arch d'elect med*, 1913, p 349, quoted by Luger (footnote 14). Rotky. *Fortschr a d Geb d Rontgenstrahlen*, vol 14, quoted by Luger (footnote 14).

22 Deery, E. M. Note on Calcification in Pituitary Adenomas, *Endocrinolog* **13** 455 (Sept-Oct) 1929.

23 Cushing, H., and Bailey, P. Tumors Arising from the Blood-vessels of the Brain. Springfield and Baltimore, Charles C. Thomas, 1928, p 25.

the reports of several cases, in most of which the tumor was found in the occipital lobe. The calcareous material is found in the walls of the anomalous vessels, the tortuous course of which is rather characteristic. Calcification is not uncommon in pinealomas and teratomas of the pineal body.<sup>24</sup>

#### CALCIFICATION IN TUMORS OF THE GLIOMA GROUP

In spite of their comparatively more rapid growth, the gliomas in many instances tend to undergo calcareous change. In this respect they are eclipsed only by congenital pituitary cysts and perhaps by aneurysms and anomalies of the blood vessels (angiomas). It is evident from our studies that the process occurs far more commonly than is usually suspected, although roentgenographic evidence of it is not always found, because calcareous material occurs in such minute particles. Van Dessel,<sup>25</sup> in a study of 1,111 cases of tumor of the brain at Cushing's clinic, found 40 that gave roentgenographic or pathologic evidence of calcareous material in their substance. Of these growths 16 were histologically verified, 9 of which were astrocytomas, 4 oligodendrogliomas, 2 neuroblastomas and 1 an ependymal glioma. Sosman<sup>26</sup> concluded that from 10 to 12 per cent of gliomas are demonstrable in the roentgenograph. Bailey and Cushing<sup>27</sup> referred in a special way to calcareous material in oligodendrogliomas and neuroblastomas.

Historically speaking, Strom,<sup>28</sup> in his treatise on intracranial calcification in general, cited the cases of Fittig and Oppenheim as the only cases of gliomas containing calcium which had been demonstrated roentgenographically. In the same year, Souques<sup>29</sup> despaired of the value of the

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<sup>24</sup> Horrax, G., and Bailey, P. Tumors of the Pineal Body. *Arch Neurol & Psychiat* **13** 432 (April) 1925. True osteomas of the brain do occur but they are exceedingly rare. They are usually small in size and are often located in the floor of the third ventricle. They should not be confused with "brain stones," masses of calcareous material probably deposited at the site of old hemorrhages or softening. Buckley recently reviewed the literature and reported a case of this kind (Buckley, R. C. Intracerebral Tumors, *Arch Neurol & Psychiat* **23** 1203 [June] 1930).

<sup>25</sup> Van Dessel, Arthur. L'incidence et la processus de calcification dans les gliomes. *Arch franco-belges de chir* **28** 845 (Oct.) 1925.

<sup>26</sup> Sosman, M. C. Radiology as an Aid in the Diagnosis of Skull and Intracranial Lesions, *Radiology* **9** 396 (Nov.) 1927.

<sup>27</sup> Bailey, P., and Cushing, H. Tumors of the Glioma Group, Philadelphia, J. B. Lippincott Company, 1926, p. 132. In a recent contribution, Bailey and Bucy (*J Path & Bact* **32** 735 [Oct.] 1929) stated that oligodendrogliomas are almost invariably calcified.

<sup>28</sup> Strom, S. Ueber die Röntgendiagnostik intrakranieller Verkalkungen, *Fortschr u d Geb d Röntgenstrahlen* **27** 577 1921.

<sup>29</sup> Souques, A. Diagnostic du siege et de la nature d'une variete de tumeurs cerebrales (psammomes ou sarcomes angiolithiques) par la radiographie, *Rev neurol* **37** 584 1921.

roentgen ray in the diagnosis of intracranial tumors, although he was able to visualize a "psammoma" by this means Heuer and Dandy,<sup>17</sup> in 6 cases demonstrated roentgenographically in a series of 100, found a growth that was probably a glioma Newell<sup>30</sup> reported 3 verified cases of glioma containing calcareous material

From a histologic standpoint, calcification has been found in gliomas by numerous investigators It was observed by Perkins<sup>31</sup> and Bielschowsky and Henneberg<sup>32</sup> in cases of more rare types of gliomas, the gangliogliomas Rosenblath<sup>33</sup> and Fraenkel<sup>34</sup> found calcareous material in the wall of glomatous cysts Olivecrona<sup>35</sup> found it but once in a series of 37 gliomas verified at operation and necropsy, and in this instance it occurred in the wall of a glomatous cyst Globus and Strauss<sup>36</sup> found calcium in one of their cases of spongioblastoma multiforme In a series of 30 cases of the same glioma, Carmichael<sup>37</sup> encountered 3 in which calcareous degeneration had occurred in the more central portions Medakovich<sup>38</sup> found calcification in 3 gliomas in a series of 24 cases Other scattered cases have been mentioned but complete descriptions are lacking or the literature is not available to us at this time<sup>39</sup>

30 Newell R R Calcification in Brain Tumors, *S Clin North America* **3** 775 (June) 1923

31 Perkins O C Ganglioglioma, *Arch Path* **2** 11 (July) 1926 Calcareous nodules were found by MacPherson in a similar tumor arising in the floor of the third ventricle (*Arch and Neurol Inst* **27** 123, 1925)

32 Bielschowsky, Max and Henneberg, R *Über Bau und Histogenese der zentralen Gangliogliome*, *Monatschr f Psychiat u Neurol* **68** 21 (March) 1928

33 Rosenblath, W Ein Beitrag zur Lehre von den Geschwulsten des Zentralnervensystems, *Deutsche Ztschr f Nervenhe* **31** 335, 1906

34 Fraenkel, Konrad Zur Pathogenese der Gehirncysten, *Virchows Arch f path Anat* **230** 479, 1921

35 Olivecrona, Herbert Die chirurgische Behandlung der Gehirntumoren Berlin, Julius Springer, 1927, p 59

36 Globus J H, and Strauss, I Spongioblastoma Multiforme, a Primary Form of Brain Neoplasm Its Clinical and Anatomic Features, *Arch Neurol & Psychiat* **14** 188 (Aug) 1925

37 Carmichael E A Cerebral Gliomata, *J Path & Bact* **31** 493, 1928

38 Medakovich, Georges Contribution a l'etude anatomique du gliome These de Paris, 1922

39 Calcification in what may be papillomas of the choroid plexus have been described by Oppenheim and Rheindorf That of Arnold seems to be an endothelioma of the choroid plexus of the third ventricle (Schuller [footnote 1 reference on p 157]) In fifty-five cases of cerebral neoplasms from Mott's laboratory Weed found calcification in twenty-two (40 per cent) (Weed, L H A Note on Calcification in Cerebral Neoplasms, *Arch Neurol & Psychiat* **6** 190, 1914) He classified the morphology of the calcified bodies as punctate vascular trabecular amorphous and periarterial Calcium was found in a third of the gliomas and in adenomas of the pituitary gland

## OUR SERIES OF VERIFIED CASES

To the present time there are 28 cases of verified gliomas in the records of the neurosurgical service of the hospital. A large number of others have been verified at operation or at necropsy but, as the tissue is not available for study, they have not been included in this series. With 2 other cases from extramural sources, we are able to report 10 histologically verified and 2 unverified cases of glioma in which calcification was demonstrable in the roentgenogram or the histologic section or both. As tissue or sections were available in the verified cases, we investigated in detail the histologic aspects of the problem.

CASE 1—*Ossification in a neuroglioblastoma multiforme*<sup>40</sup> (*spongioblastoma multiforme*) in the body of the corpus callosum

The patient, a Mexican girl, aged 18, was admitted to the hospital in coma on April 26, 1926. Seven years prior to the onset of the present illness, the patient had spells of vomiting associated with severe headaches for a period of three months. During this time there was a gradual failure of vision, which resulted in complete blindness. At the end of the period all symptoms cleared up without treatment, the patient remaining well until two weeks before admittance to the hospital. At this time the headaches recurred. Three days before coming into the hospital, she began to have generalized convulsions and vomiting.

On examination the patient appeared to be in deep coma marked by frequent convulsive seizures of the right side of the body and conjugate deviation of the head and eyes to the right. She was rather obese, the distribution of the adiposity resembling that seen in pituitary disturbance. The pupils were widely dilated, and bilateral secondary optic atrophy was found. A lumbar puncture showed the spinal fluid to be under increased pressure. Laboratory analysis revealed a two plus Wassermann reaction and a paretic type of colloidal gold curve.

Stereoscopic films revealed a small round mass of calcification lying just above and slightly posterior to the sella turcica in the midline of the skull (fig. 1).

The patient remained about the same during the period of observation in the hospital. She died rather suddenly before surgical exploration was attempted.

At necropsy, a fairly circumscribed tumor was found in the midline of the brain and extending down into the third ventricle, apparently having its origin from the inferior part of the body of the corpus callosum. A compact mass of bone was found in the tumor. Histologic studies revealed firm, scarlike tissue about the bony mass, while in the peripheral portions a loosely arranged tumor stroma was found containing cells typical of neuroglioblastoma multiforme.

*Comment*—It seems apparent that seven years prior to the illness which brought about the death of the patient a rapidly growing tumor developed from the tissues of the corpus callosum which after a

<sup>40</sup> We have come to indicate the tumor, commonly known as 'gliosarcoma' or more recently as "spongioblastoma multiforme" as a neuroglioblastoma. In a histologic study of a series of cases in this laboratory we found typical and well developed neuroblasts as well as glioblasts. The primary cell must therefore be bipotential as is the case in the essential elements of the medulloblastoma cerebelli. A complete report is to appear soon.

fulminant course of three months, suddenly ceased to grow for some unaccountable reason. The necrosis which took place at that time probably was the starting point for the formation of bone, as was described by Mallory<sup>41</sup>. A renewed growth of the tumor came about, which hastened the death of the patient after a short course of eight weeks. This was the only case in the series in which actual bone was found.

*CASE 2—Multiple calcareous nodules in an atypical glioma of the left frontal lobe*

A linotype operator, aged 45, was admitted to the hospital on Sept 9, 1926, complaining of headaches, vomiting, failing vision and weakness in the right arm and hand, all of six months' duration.



Fig 1 (case 1)—Mass of calcification above the sella turcica. At necropsy this proved to be bone formation within a neuroglioblastoma multiforme of the corpus callosum.

At the time of admittance the patient was found to be rather somnolent and presented a bilateral choked disk, more marked on the left side, associated with weakness of the right side of the face and spastic paralysis of the right arm. The deep reflexes were increased on the right side, and Babinski's sign was present on this side. There was also a slight tremor in the left extremities and left ankle clonus.

Stereoscopic films of the skull showed numerous small calcareous particles scattered throughout the left frontal region. There was an associated thinning of the frontal bone on the left side (fig 2).

<sup>41</sup> Mallory, F. Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1914, pp. 355, 444 and 627.

A left frontal exploration was undertaken on September 30, and a soft, infiltrating glioma was exposed which seemed to fill the entire left frontal lobe. The patient's condition was critical, so complete removal was not undertaken. He died a few hours later.

As necropsy was refused, the exact extent and relationships of the tumor were not determined. The tissue removed at the time of operation was reddish gray and soft and it contained numerous small calcareous particles. Histologic studies showed the tumor to be rather cellular, the nuclei of the constituent cells being more uniform in size than is usually encountered in malignant invasive gliomas of the cerebral hemispheres. In architecture and cellular detail it resembled more nearly medulloblastoma. No further tissue being available at the time of this study, a determination of its exact nature could not be made.

*Comment*—The distribution of the calcareous particles in this case was interesting, as they were found throughout the entire left frontal



Fig 2 (case 2)—Diffuse calcification in a glioma of the left frontal lobe

region. In no other case in our series was such a uniform involvement of the tumor tissue found.

*CASE 3—Calcification in a fibrillary astrocytoma of the left parietal lobe*

A Negro chauffeur, aged 26, was admitted to the hospital on July 20, 1927, with the complaint of left sided fronto-occipital headaches, vertigo and, for the past three months, double vision and failing vision. In the past year he had two generalized convulsions. His condition grew steadily worse in spite of a submucous resection and anesthetization of the sphenopalatine ganglion.

On examination bilateral choked disk was found associated with a bilaterally diminished visual acuity. Aside from a slight weakness of the right hand there were no other positive neurologic observations. Lumbar puncture revealed the cerebrospinal fluid to be under greatly increased pressure but otherwise normal.

Stereoscopic films of the skull showed a large number of calcified particles in the posterior parietal region on the left side associated with a thinning of the vault over the calcified area (fig 3).

A left osteoplastic flap was turned down on July 28, 1927, and an underlying tumor could be seen through a thinned dura. When the dura was opened, a large cyst ruptured spontaneously. A firm, well delineated tumor was entirely removed by blunt dissection. After a somewhat stormy postoperative course, the patient made a complete recovery.

At the time of the last examination, over two years after the operation the patient was free from symptoms and worked every day. Roentgenographic examination of the skull revealed no further evidence of calcification.

The tissue removed at operation was rather firm, friable and reddish, and it contained numerous calcareous particles. Histologic studies showed that it was comparatively acellular and had a stroma characteristic of a fibrillary astrocytoma.

*Comment*—The clinical course was rather short for an astrocytoma. The calcareous particles, found particularly in the margin of the tumor,



Fig. 3 (case 3)—Flocculent calcification in an astrocytoma fibrillare of the left parietal lobe.

served to delineate it very well on the roentgenogram. Complete extirpation was apparently done in this case and the prognosis was good.

*CASE 4—Calcification in a neuroglablastoma multiforme of the right frontal lobe.*

A cabinet maker, white, aged 42, was admitted to the psychopathic ward of the hospital for observation. His wife stated that he had been undergoing marked mental changes for the past six months, had complained of headaches for the past five weeks and more recently had spells of weakness and double vision. At admission to the hospital, he had two Jacksonian convulsions involving the left side of the body.

On examination the patient presented marked mental changes, demonstrating typical "Witzelsucht" as described in tumors of the frontal lobe. The disks showed bilateral chokring, and there was bilateral anosmia. Some ataxia, past-pointing of the left arm and a Babinski sign on the left were observed.

Stereoscopic films of the skull failed to reveal any evidence of intracranial disease

After careful study, the patient was transferred to the neurosurgical service. On March 22, 1928 a ventricular puncture was done and air injected. Ventriculograms showed a filling defect of the anterior horn of the right lateral ventricle. A right frontal exploration was attempted on May 10, but had to be abandoned because of the critical condition of the patient. A reexploration a month later revealed an extensive infiltrating glioma of the right frontal lobe, a large portion of which was resected. The patient died five days after operation. Necropsy was refused.

The tissue that was removed at operation was subjected to study and the tumor proved to be a neuroglia blastoma multiforme. Small calcareous particles were found in the margin of the tumor.

*Comment*—This is another case in which the roentgenograms failed to reveal any evidence of calcification, yet in which the process was clearly shown by microscopic study of the tumor tissue.

*CASE 5—Calcification in an astrocytoma protoplasmaticum of the left temporo-parietal region*

A white laborer, aged 36, was admitted to the hospital on Oct. 26, 1928, with the complaint of headaches, vomiting, loss of weight and progressive failure of vision of eight months' duration.

At the time of admittance the patient showed marked mental retardation and confusion, he was unable to give a clear account of the history of his illness. He was practically blind, having but a slight degree of light perception in the right visual fields. The pupils were widely dilated and unequal, the right being larger than the left. The optic disks showed a bilateral choking of 5 diopters' elevation. There was a slight right hemiparesis associated with an increase in the deep, and a decrease in the superficial, reflexes on the same side.

Stereoscopic films of the skull revealed flocculent masses of calcareous material in the posterior temporo-parietal region of the left side (fig. 4).

On November 15, a left osteoplastic bone flap was turned down and a decompression made. Because of the condition of the patient, further exploration could not be done at the time. Two weeks later the region was reexplored, and a large mass of soft, gelatinous tumor tissue containing calcareous particles was removed. After a somewhat stormy postoperative course, the patient recovered and was discharged on Feb. 15, 1929.

Because of elevation of the bone flap, he was readmitted to the hospital on October 8. At that time a marked weakness of the right arm and leg was noticed. Stereoscopic films of the skull showed the bone flap markedly elevated and riding on the soft tissue swelling at the site of decompression. Calcareous particles were found both within the skull and in the soft tissue mass protruding through the operative defect. On October 17, a reexploration was done and another large mass of soft gelatinous glioma was resected. When the patient was ready for discharge from the hospital, he showed residual right-sided weakness and almost total blindness.

The tissue recovered at both operative sessions proved to be comparatively acellular and had a stroma of faintly fibrillary character, characteristically of a protoplasmic astrocytoma. Numerous calcareous masses were found throughout the tissue.



*Comment*—This rather benign tumor was superficial in its situation, so that it was exposed when the dura was opened. Its extent was well marked in the roentgenogram by the contained calcareous particles, which proved of value to the surgeon when he attempted extirpation. Such cases should have an increasingly good prognosis with the aid of electrosurgical methods.

CASE 6—*Calcification in a neuroglablastoma multiforme arising in the genu of the corpus callosum*

A stenographer, white, aged 30, divorced, was admitted to the neurologic service of the hospital on Oct. 4, 1928, with the complaint of ringing in the right ear for six months, generalized convulsions and an ataxic gait for four months. More recently, she had complained of severe headaches and had become incontinent. She had become steadily worse since the onset of her illness, and at the time of admittance she showed drowsiness deepening into stupor.



Fig. 4 (case 5)—Calcification in an astrocytoma protoplasmaticum of the left temporoparietal region.

On examination the patient appeared stuporous, but could be aroused to some extent. Marked mental changes had occurred. The patient was stubborn and refused to answer questions. The pupils were irregular and unequal, the right being larger than the left. The disks were bilaterally edematous, with an elevation of 4 diopters. The extra-ocular muscles on the left side were weak, so that there was little control of movement of the left eyeball.

Stereoscopic films of the skull showed no evidence of intracranial disease.

A lumbar puncture revealed a clear fluid under increased pressure. A ventricular puncture was attempted, but, because of the condition of the patient had to be abandoned before air was injected. The patient died six days after admittance.

Necropsy revealed a large grayish invasive glioma arising from the genu of the corpus callosum and extending into both frontal lobes. Histologic studies of its tissue showed it to be a typical neuroglablastoma multiforme. Small particles of calcareous material were found in the tumor tissue, particularly near its margin.

*Comment*—This case further illustrates the fact that calcification may occur within ghomas without its being demonstrated in the roentgenogram. This may not necessarily be because the films are not clear or are improperly taken, but rather because the calcareous particles may be so small as not to be visualized. In any case when an intracranial tumor is suspected, it is important to have stereoscopic pictures in which details can clearly be made out, so as not to overlook any evidence of value in the diagnosis.

*CASE 7—Calcification in a neuroglioblastoma multiforme of the left parietal lobe*

A pipefitter, white, aged 49, was admitted to the hospital on Nov. 3, 1928, with the complaint of headaches, vomiting and generalized convulsions of a year's



Fig. 5 (case 7) —Calcification in a neuroglioblastoma multiforme of the left parietal lobe

duration, with recent failure of auditory acuity and mental confusion. The symptoms had progressed in severity from the onset, and it was noticed on the day of admission that the vomiting was definitely projectile.

Examination revealed the patient to be mentally disturbed and totally deaf. The pupils were unequal, the right being larger than the left. There was bilateral choked disk of 4 diopters' elevation. The vestibular responses showed bilateral hypersensitivity, associated with a complete loss of hearing. The deep reflexes were generally increased, and a bilateral Babinski sign was present.

Stereoscopic films of the skull showed flocculent calcareous shadows on the left side of the intracranial space beneath the parietal bone. There was no destruction of the bone in this region, and there were no other positive observations (fig. 5).

Ten days after admittance to the hospital, a left osteoplastic flap was turned down. The dura was found to be under marked tension, and because of the condition of the patient, it was not opened. He died on the day following operation.

At necropsy a yellowish-gray, somewhat degenerated, invasive glioma containing calcareous particles was found involving the left parietal lobe. Microscopic study of the tissue showed it to be a neurohablastoma multiforme.

*Comment*—This case is of particular interest in that the neurologic symptoms and signs were extremely misleading. The marked pressure signs, with bilaterally and equally choked disks and bilateral deafness suggested a lesion of the posterior fossa, possibly a tumor of the pineal body. The diagnosis was accurately made from the roentgenograms of the skull.

CASE 8—*Calcareous masses in an ependymal glioma of the left occipital globe.*

A Mexican girl, aged 6, was admitted to the service of contagious diseases, with the provisional diagnosis of encephalitis. A clear history of the illness was not obtained, but the child had been ill for about a month before coming to the hospital. She suddenly became comatose, and two days later was admitted.

On examination, the child appeared deeply comatose. The left pupil was widely dilated and there was evident weakness of the extra-ocular muscles on the left side. There were no other positive neurologic observations. Lumbar puncture revealed that the spinal fluid was clear and contained 60 lymphocytes per cubic millimeter. There was also a trace of globulin.

The child died before roentgenographic studies could be made.

At necropsy a large multilocular cyst occupying the entire posterior portion of the left hemisphere was found, containing yellow coagulable fluid. A mural nodule about the size of a walnut was situated on the medial wall of the largest cyst. In the central portion of the tumor, large calcareous masses were encountered. These felt like particles of bone and were limited in extent to this single portion of the tumor.

*Comment*—This is the only case of an ependymal tumor of the series in which calcareous material was found. It is also of interest to note the situation of the tumor in the left occipital region. It probably had its origin from ependymal rests derived from the posterior portion of the lateral ventricle. Van Dessel also reported a case of ependymal tumor in which calcification had occurred.

CASE 9—*Calcification in an invasive neurohablastoma multiforme of the left frontal lobe.*

A housewife, white, aged 38, was admitted to the service of Dr. Carl W. Rand at the Good Samaritan Hospital. She gave a history of right-sided convulsive seizures of five and one-half years' duration, associated occasionally with periods of unconsciousness. The condition grew steadily worse, so that in recent months the patient had difficulty with speech following the convulsive seizures.

On examination the patient appeared rather nervous and emotionally unstable. The eye grounds showed filling of the optic cups and a fulness of the retinal veins. There was a definite weakness of the right arm and leg associated with an increase in the deep reflexes, a Babinski sign and ankle clonus on that side. There was also a decrease in sensation on the entire right side of the body.

Stereoscopic films of the skull did not reveal any evidence of intracranial calcification.

A diagnosis of left frontal tumor was made, and an exploration revealed an invasive glioma of the left frontal lobe which was only superficially resected. The patient died a few days later.

The brain was removed by Dr. Roy W. Hammack, pathologist to the Good Samaritan Hospital. There was an extensive infiltrative, poorly delineated glioma of the left frontal lobe which seemed to originate from the anterior portion of the corpus callosum, spreading into the left hemisphere. Histologic studies showed it to be a neuroglioblastoma multiforme with very small calcareous particles in its margin and in the adjacent brain tissue.

*Comment*—This case is interesting in that it had a long course for the type of tumor found at necropsy. The small particles of calcareous material failed to be visible in the roentgenograms of the skull as in two



Fig. 6 (case 11)—Solid calcified mass in a presumed glioma of the left parietal region.

of the previously reported cases. Of special interest was the fact that most of the calcification occurred in the adjacent part of the brain rather than in the tumor itself.

*CASE 10—Calcification in a fibrillary astrocytoma of the right cerebellar hemisphere*

A boy, aged 10, came under the care of a private physician, Dr. Dee M. Rees, who furnished us with a history of the case and with the pathologic specimen. Four years prior to his present illness, the patient had a period of severe headaches associated with vomiting and obstinate constipation. After an illness of four months the symptoms cleared up and aside from slowness in learning at school, the child seemed to be normal. In October, 1929 there was a recurrence of the headaches which seemed to have a fronto-occipital situation and which

were again associated with vomiting. He developed a ravenous appetite, which, together with alternating constipation and diarrhea, led numerous observers to make a diagnosis of intestinal worms, for which he was treated.

On examination, the child appeared somewhat emaciated and not very alert. The forehead seemed more prominent than usual, and the entire head was enlarged. The pupils were dilated and equal and reacted sluggishly to light. There was a lateral nystagmus, particularly to the left. All the deep and superficial reflexes were abolished. The limbs were rigid, particularly the lower extremities, the neck was stiff and there was a positive Kernig sign on the left side.

The child died shortly after coming under the observation of the referring physician and before roentgenographic studies could be made.

At necropsy, the brain was found to be much congested, the convolutions flattened and the lateral ventricles much dilated with clear fluid. In the right cerebellar hemisphere was a firm, fairly well delineated tumor, about 4 cm. in diame-



Fig 7 (case 12) —Solid mass of calcification in a possible slow growing glioma of the left temporal lobe

ter, with central softening. About the softened area were numerous calcareous particles which gave a gritty feel to the cut surface of the tissue. The peripheral portion seemed to be free from calcification.

The heart and lungs appeared normal on gross examination, the bowel was much thickened and its lumen gave evidence of chronic inflammation. The thymus was enlarged and the lymph nodules were generally hypertrophied.

*Comment*—This case is unusual in that it is the only one in the series in which a tumor was situated beneath the tentorium. Tumors in the posterior fossa because of their tendency to cause hydrocephalus probably bring about death before calcification takes place even though they are essentially benign and of slow growth. It is likely that in this case the tumor had begun its course four years previously, and for some unknown reason had become quiescent and had undergone calcareous-

degeneration With a resumption of its growth activities there was a recurrence of symptoms which brought about the death of the patient As far as we have been able to determine there has been no other case reported in which a calcified glioma was found in the posterior fossa <sup>42</sup> It is to be regretted that no roentgenographic studies were made

#### UNVERIFIED CASES

The following cases are described because of the special interest of the clinical history and the roentgenograms of the skull even though the tumors were not verified histologically Van Dessel and Fraenkel

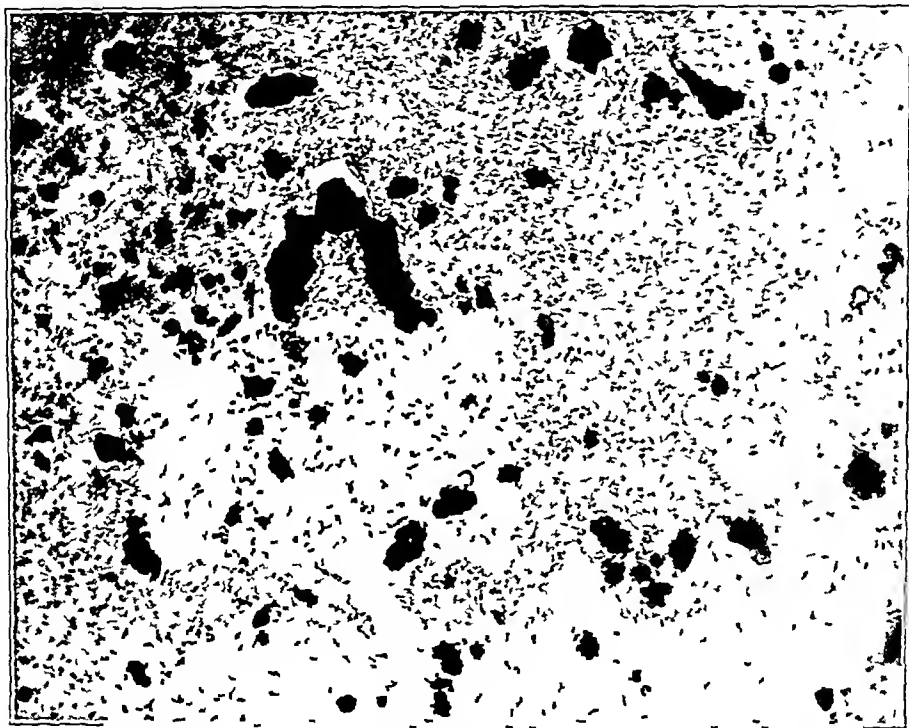


Fig 8 (case 5) —Calcareous masses scattered more or less evenly throughout the tissue of the tumor Hematoxylin and eosin,  $\times 95$

mentioned the occurrence of calcification within the walls of glomatous cysts the former author reporting two which were evacuated at the time of operation We are unable to say whether these tumors were solid or cystic, because they were deep within the substance of the hemisphere

<sup>42</sup> In 1899 Church reported a case of cerebellar tumor which he claimed to have demonstrated by the roentgen ray This has not met with universal acceptance because the glioma exposed at necropsy did not contain calcium and, from the roentgenogram shown in his article it is doubtful if the opaque area represented the tumor (Church A Cerebellar Tumor Recognized Clinically, Demonstrated by the X-Ray and Proved by Autopsy Am J M Sc **117** 125 [Feb] 1899)

CASE 11—*Calcification in a presumed glioma of the left parietal region*

A Mexican girl, aged 15, was admitted to the neurologic service of the hospital on Jan 28, 1929. She complained of headaches, vomiting and progressive failure of vision of one and one-half years' duration. During this period she had two convulsive seizures of a generalized character.

When first examined, the patient was completely blind. The pupils were widely dilated and reactionless. A bilateral primary optic atrophy, more marked on the left side, was present. There was a complete right hemiparesis associated with increased deep reflexes, ankle clonus and a Babinski sign on that side. Sensation was also diminished on the right side, and a suggestive astereognosis of the right hand was noted on repeated examinations.

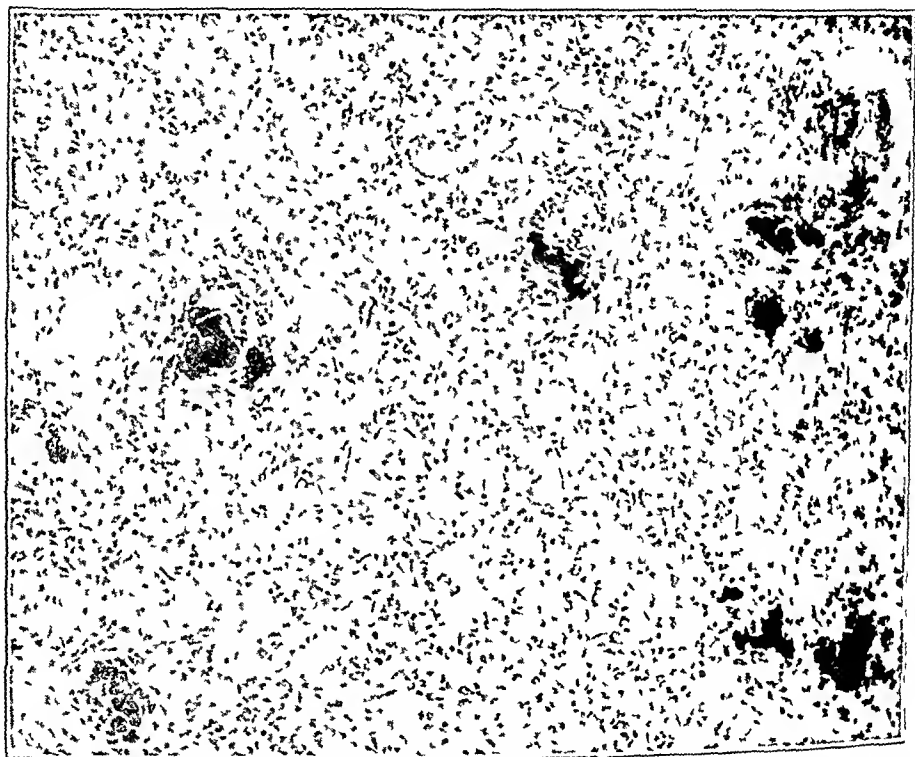


Fig 9 (case 7)—Localized masses of calcification scattered throughout the tumor tissue. Hematoxylin and eosin  $\times 180$ .

Stereoscopic films of the skull revealed a small, rather sharply defined area of calcification deep in the left parietal lobe (fig 6).

On June 30 a left osteoplastic bone flap was laid down, but no tumor was seen superficially. The patient's condition was poor, and the operation had to be concluded. The patient's family refused to consider further operative procedure and she was discharged after an uneventful recovery. She returned on several occasions to the clinic but there was no further change in her condition except for some bulging of the decompression area.

*Comment*—It is to be regretted that tissue could not be recovered from the lesion to verify the diagnosis. The growth was probably a deeply seated slowly growing glioma.

CASE 12—*Calcification in a possible glioma of the left temporal lobe*

A Mexican woman, aged 27, was transferred from the otorhinolaryngology service of the hospital. She had been under observation for acute frontal and maxillary sinusitis having complained of pain in the left side of the head associated with generalized convulsions for three years. A right hemiplegia of gradual onset had been present since the age of ten.

Examination disclosed a marked right-sided hemiplegia, associated with an increase in the deep, and a decrease in the superficial, reflexes. A definite Babinski sign was present on the right side and a suggestive one on the left. Perimetric examination demonstrated the presence of a right homonymous hemianopia.

Stereoscopic films of the skull showed a compact mass of calcification in the region of the left temporal lobe (fig. 7).

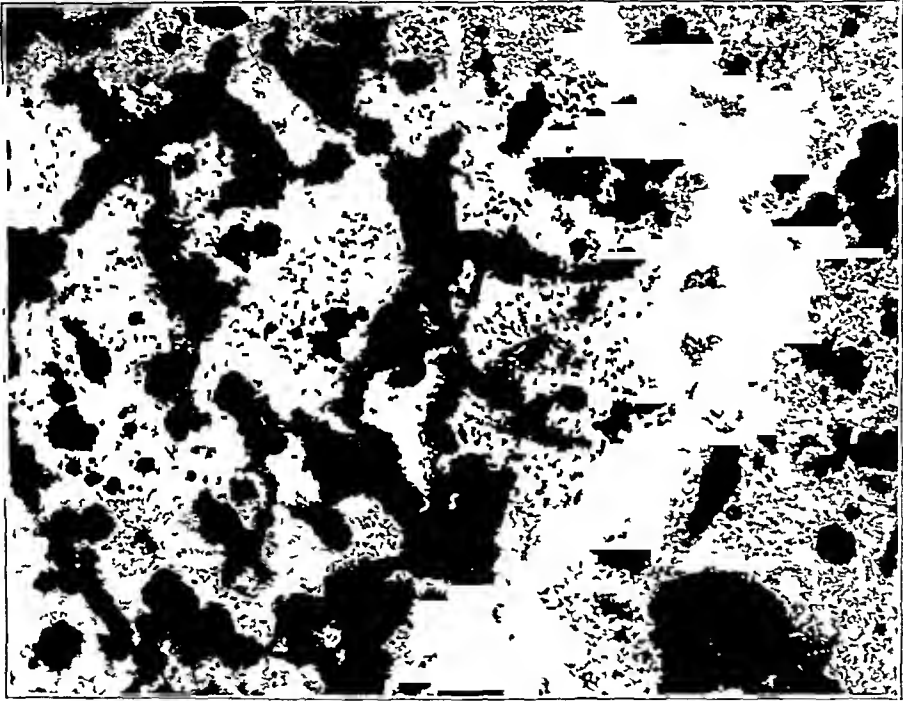


Fig. 10 (case 10)—Masses of calcareous material in the central portion of a cerebellar astrocytoma. Hematoxylin and eosin,  $\times 95$ .

A left osteoplastic flap was turned down on July 11, 1928. The calcareous mass could be palpated through the overlying cortex but owing to the patient's poor condition, a decompression opening was made and the wound closed. The patient made an uneventful recovery and was well when last examined.

*Comment*—This case also lacks positive verification of its true nature. Because of the left-sided headaches, the homonymous hemianopia and the right hemiplegia of slow onset we assume that it was a neoplasm, possibly a glioma.

## THE PROCESS OF CALCIFICATION IN THE GLIOMAS

The deposit of calcium within the body tissues is dependent on some chemical change which favors the precipitation of blood calcium. The



calcium salts of the blood are held in simple solution or in combination with protein substances. This suspension or combination, evidently an unstable one, may be altered by variations in the hydrogen ion concentration of the tissues, changes in the carbon dioxide tension, or perhaps by qualitative or quantitative changes in the salts themselves, as was suggested by Wells<sup>43</sup>. This author further believes that necrosis, hyaline change and an enfeebled circulation are also factors in the process. It is also possible that such regressive changes in the involved tissue result in the formation of some calcium-binding substance, such as phosphoric acid or the fatty acids. This is significant in view of the occurrence of



Fig. 11 (case 1) — Bone formation in a neuroglia multiforme of the corpus callosum. Hematoxylin and eosin,  $\times 95$ .

calcium deposit in those parts of the glioma which have undergone a degree of fibrosis.

The necessity of this predisposing degenerative process was accepted by van Dessel in his study of calcification in the gliomas. He observed the presence of hyaline changes in the walls of blood vessels in which calcium was deposited. This is in accord with the view of Mallory<sup>44</sup> who considered hyaline change in the blood vessels as necessary for the deposition of calcareous material. In our cases we were struck with the almost complete absence of hyaline change, there was very little

<sup>43</sup> Wells H. G. Chemical Pathology. Philadelphia W. B. Saunders Company, ed. 5, 1925, p. 486.

evidence of any other type of regressive process. As previously stated the calcareous masses were inclined to be more common in areas where a certain degree of fibrosis had taken place. Whether this is a coincidental or an associated observation is not possible to settle at this time. In a few instances minor hyaline changes in the walls of the blood vessels, as indicated by a loss of tissue morphology, were observed but never to the degree described by van Dessel. From our observations it seems evident that the essential factor must be an interference with local tissue respiration which may take place without any alteration in tissue structure.

The distribution of the calcareous particles within the gliomas varied greatly in the different cases as observed under low power magnification.

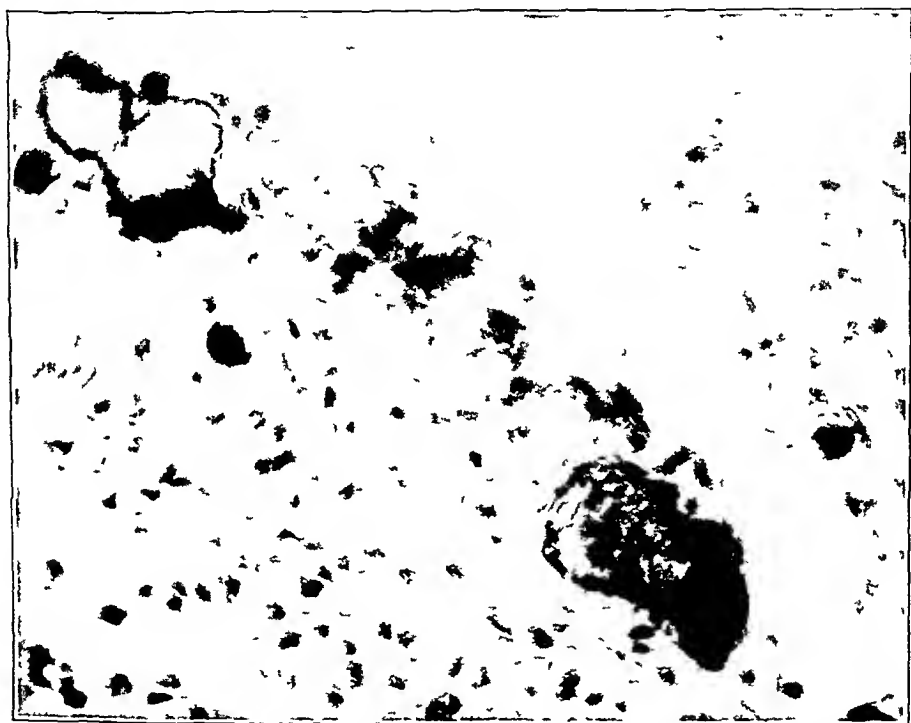


Fig. 12 (case 5)—Colloid globules in the wall of a blood vessel in which calcification is taking place. Hematoxylin and eosin,  $\times 350$ .

In some instances, it was fairly evenly distributed throughout the tumor tissue (figs 8 and 9), in others it was bunched together or confined to one or two larger masses in a single situation (fig 10). In one glioma a large central mass proved to be actual bone (fig 11).<sup>44</sup> This irregu-

<sup>44</sup> Actual bone formation in tumors of the intracranial structures is apparently a very rare occurrence. The only cases that we have found cited in the literature are those referred to by Oppenheim—a partly ossified tumor of the cerebral hemisphere and bone formation in a glioma (Oppenheim H. *Die Geschwulste des Gehirns*, ed 2. Nothnagel. *Handbuch der speziellen Pathologie* 1903 quoted by Schuller [footnote 1]).

lar distribution accounts very likely for the comparatively low percentage of calcified gliomas found at operation, the calcareous particles being situated in the remaining deeper portions of the tumor. In the neurogliaomas of our series, the more cellular and rapidly growing portions contained no calcium, while the more fibrous and acellular areas were studded with calcifications.

The calcification was found most characteristically in the adventitia or media of the blood vessels. In no instance was it found in the intima, although droplets of calcium were observed on one occasion within a group of blood cells within the lumen. The situation of the deposit would suggest that the process rarely takes place in actual con-

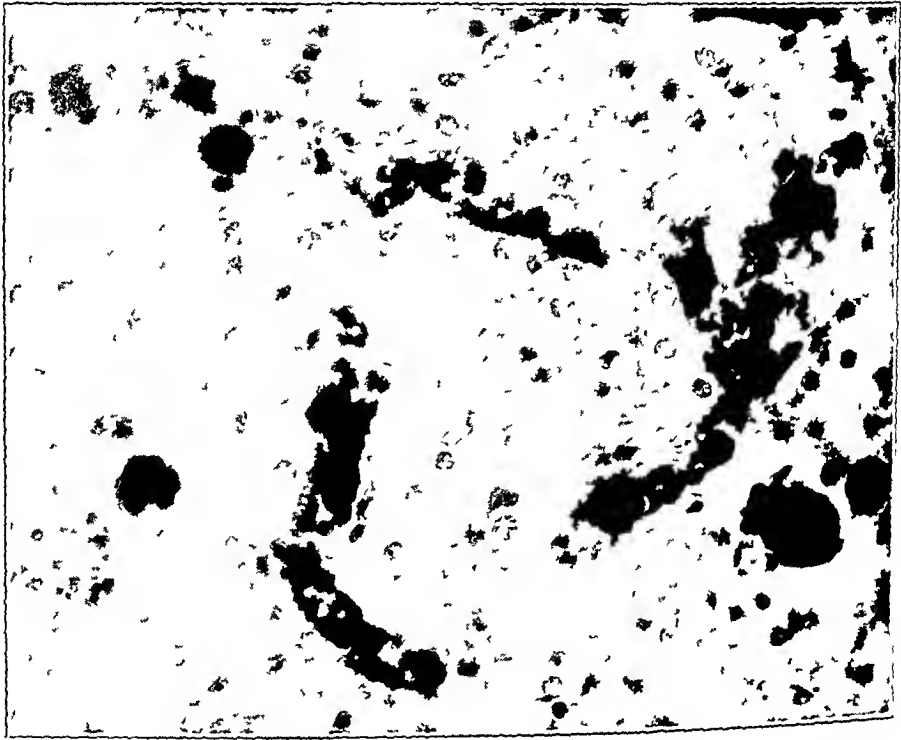


Fig 13 (case 5) —Spotlike calcification marking the course of capillaries in the margin of the glioma. Hematoxylin and eosin,  $\times 350$

tact with the circulating blood, but rather in tissues somewhat removed from it. It also suggests that calcification usually is not primary in the tissue where an active circulation of the tissue fluid is taking place but that in these areas it is usually secondary and spreads outward from the vessel.

The preliminary stage in the process, at least in the larger vessels, was the appearance of small round shotlike globules in the media (fig 12). Mallory<sup>45</sup> referred to the presence of these droplets which precede the actual deposit of calcium and considered them to be of a colloidal nature. In the smaller vessels and capillaries, the droplets of calcareous

<sup>45</sup> Mallory, F. A Contribution to the Study of Calcareous Concretions. *Brain J. Path. & Bact.* 3:110, 1896.

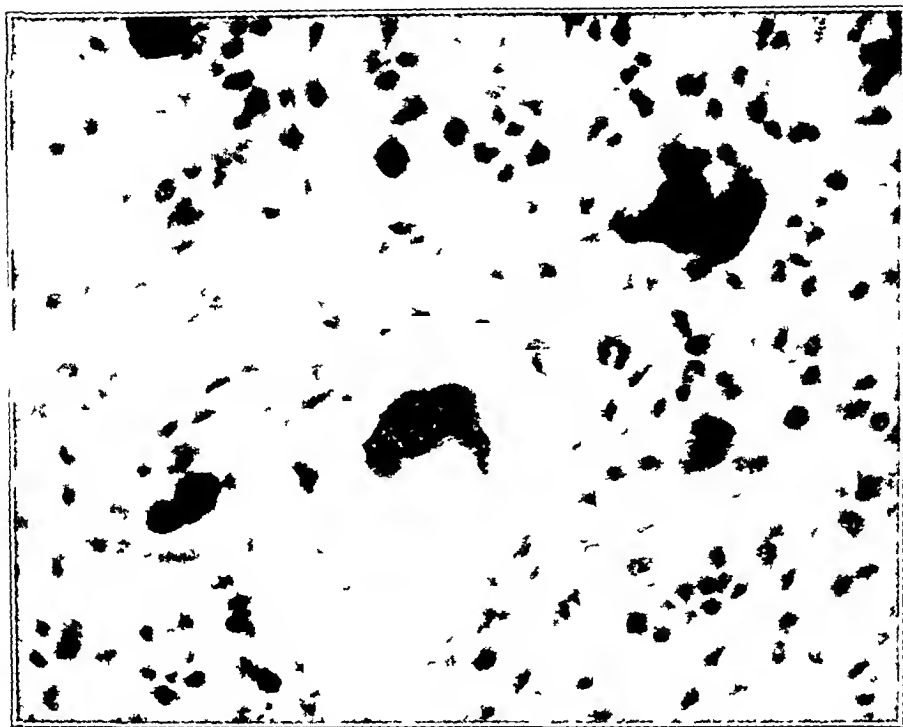


Fig 14 (case 5) —Calcification of the wall of the blood vessel forming a ring. The lumen is also occluded. Hematoxylin and eosin.  $\times 350$

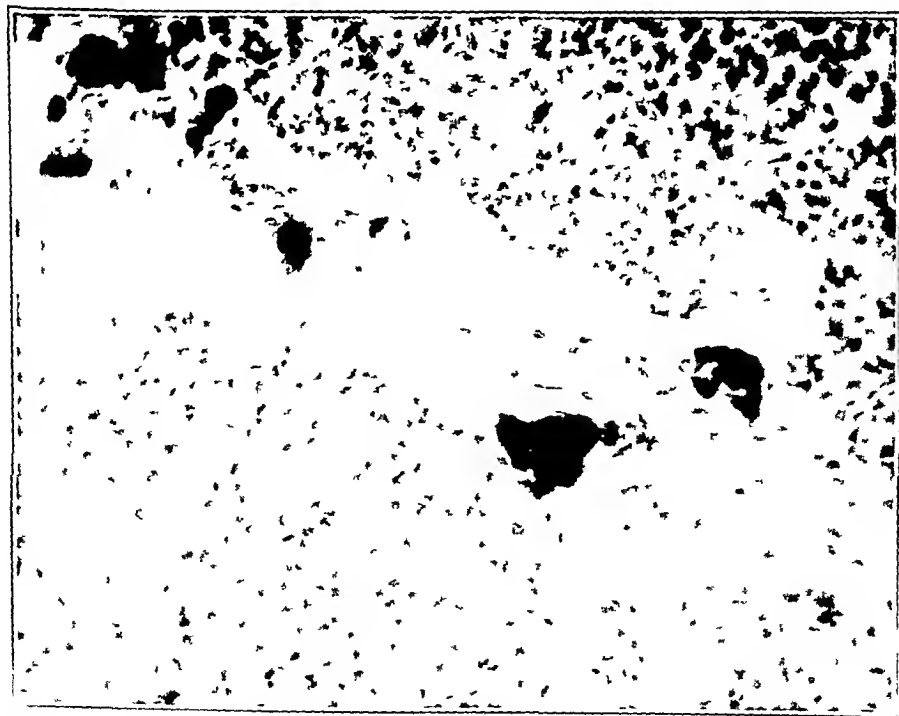


Fig 15 (case 7) —Masses of calcareous material in the adventitia of a small blood vessel. Hematoxylin and eosin.  $\times 220$

material appear as round individual or coalesced globules which marked the course of the involved vessels through the tissue (fig 13). In a further stage, coalescence of the globules converts the vessel into a rigid tube best seen in cross-section as a ring of calcium (fig 14). Complete occlusion of the lumen may follow. In the smaller vessels, where distortion may take place easily, the lumen may be obliterated early, appearing as a small solid mass of calcareous material. Where some of the larger vessels have been sectioned longitudinally, small masses of calcium are observed here and there in their course (fig 15). In our case of calcification in an ependymal glioma, the calcified vessels formed a veritable meshwork in a central fibrosed area (fig 16). This is suggestive of the process described by Bassoe and Hassin<sup>46</sup>.

In one case, small shotlike particles of calcareous material were found scattered throughout the tissue, having no particular relationship to its vasculature. In this case, corpora amylacea were observed, some of which were undergoing calcification (fig 17).

The process occurs less frequently and characteristically within individual tumor cells. Either the nucleus or the protoplasm of the cell may be the seat of small globules of calcium. Whatever the original situation may be, it tends to expand peripherally so that the entire cell is filled with a spherical mass. When starting in the protoplasm, which seems to be the more common point of origin, the nucleus is found crowded to the periphery of the cell in the form of a crescent. When the process occurs in a group of cells, it gives the appearance of a bunch of grapes (fig 18).

The deposit of calcium in the stroma as a primary process was unusual. We observed it in a few isolated places in which small globules were found outside of a cellular structure and within the fibrillary stroma. This phenomenon may be accounted for by the comparatively less demand for active metabolic activity on the part of the stroma. Calcium was found in a few instances within extravascular masses of blood cells.

The association of calcification with small cystic cavities at the margin of slower growing neurogliaomas was observed in two cases. The cysts are probably the result of tissue liquifaction incident to an interference with the local blood supply. In the cases studied, the calcareous particles were confined to the margin of the tumor and the adjacent brain tissue, none being found in its more central portion. The small particles were found largely in the walls of the capillary blood.

46 Bassoe P. and Hassin, G. B. Calcification of the Cerebral Vessels. *Journal of Clinical Picture Simulating Brain Tumor*, Arch Neurol & Psychiat 6: 351 (Oct. 1921) figure 2.



Fig. 16 (case 9) — Meshwork of calcified blood vessels in the central portion of an ependymal glioma. Hematoxylin and eosin,  $\times 95$ .

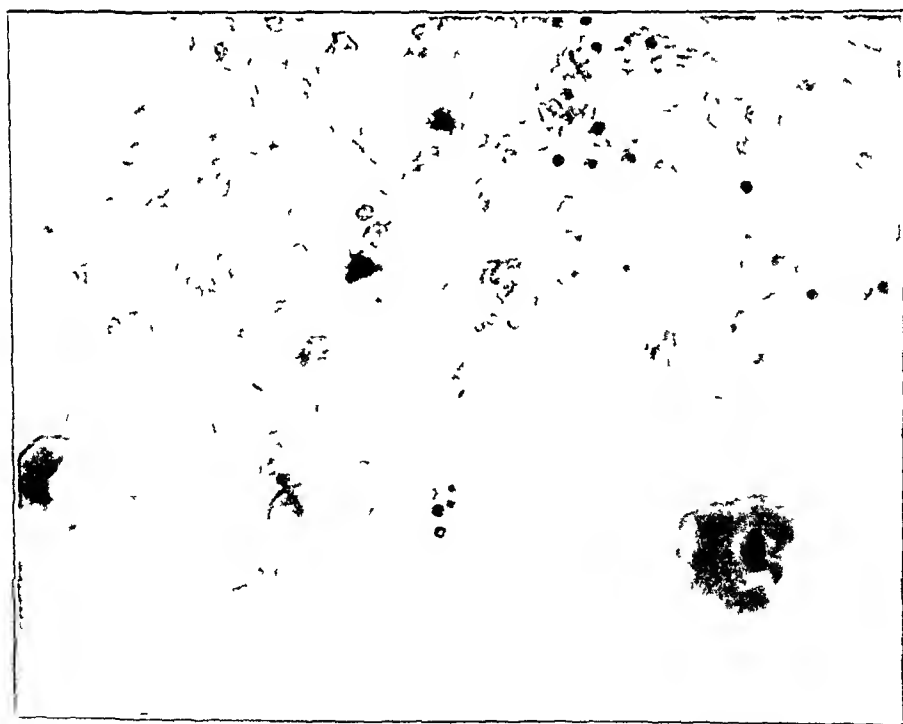


Fig. 17 (case 3) — Calcification occurring in a corpus amyloideum. Spotlike calcifications are also seen scattered throughout the tissue. Hematoxylin and eosin,  $\times 700$ .

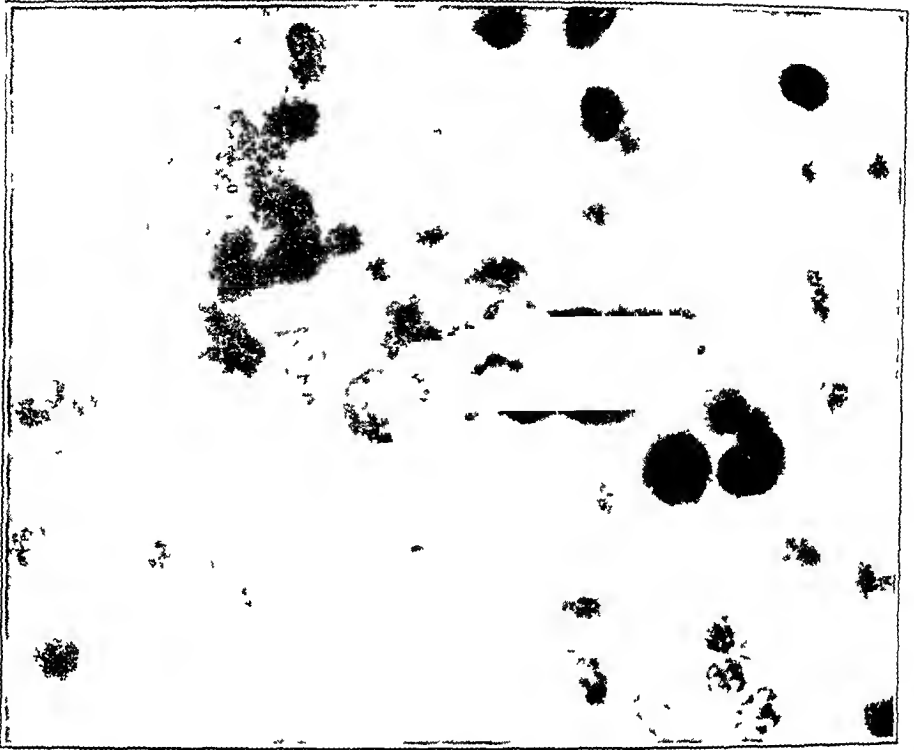


Fig 18 (case 7) —Calcareous degeneration taking place in a group of tumor cells Hematoxylin and eosin,  $\times 885$

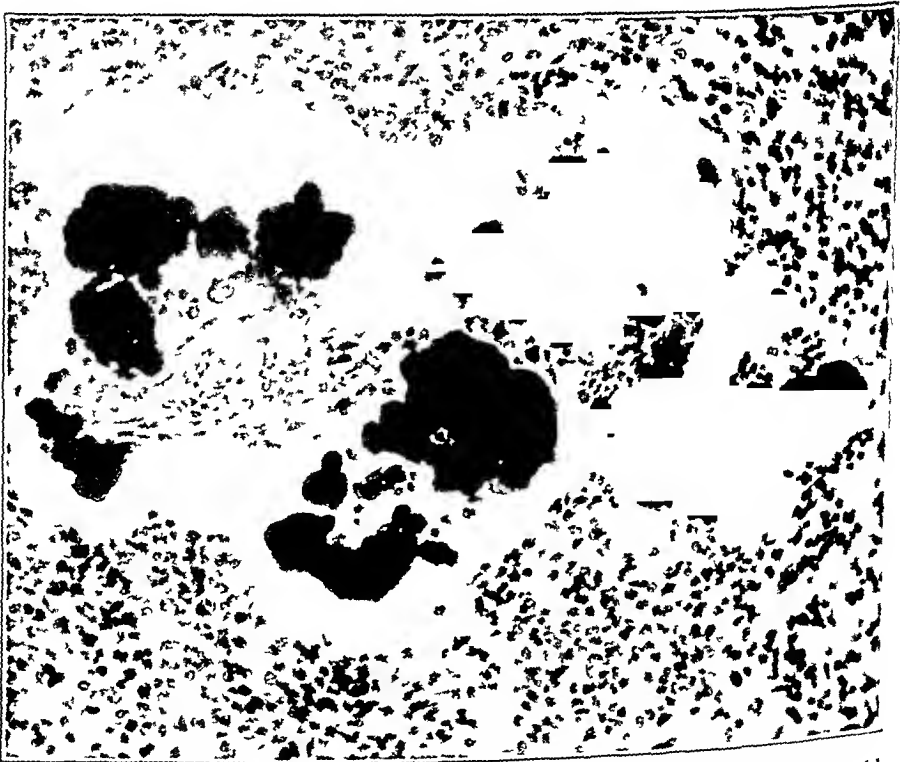


Fig 19 (case 7) —Showing the relation of the calcareous masses to a blood vessel Hematoxylin and eosin,  $\times 220$

vessels. Its small bulk was further emphasized by the fact that a review of the roentgenograms showed no evidence whatever of its presence. Whenever the margin of the tumor appears spongy in the gross specimen, it is possible that such calcareous deposits will be found. This seemed to be the case in a glioma of this type studied by Medakovich.<sup>48</sup>

In the brain tissue at the margin of the tumor in our cases, the process seemed to be confined entirely to the walls of the blood vessels. Careful study of the ganglion cells undergoing regressive changes revealed no deposit of calcium. We interpreted this to mean that the degenerative process was taking place too rapidly or that the other factors were absent. Landau<sup>47</sup> reported the occurrence of spotlike calcification in the blood vessels and the ganglion cells at the margin of a diffuse glioma.

A review of the question of calcification within the tissues of the brain shows that numerous conditions may bring about an alteration of the respiratory exchange favoring the deposit of calcium. This change seems to affect most characteristically the walls of the blood vessels but may extend out to involve the elements of the nervous system. In this sense a glioma may be considered as one of the factors that interfere with the respiratory activity to the extent that calcium is deposited. This is true particularly when it is recognized that the blood vessels of the glioma are probably those of the preexisting brain tissue the space of which the tumor has come to occupy, although some are also newly formed. Strength is added to the argument by the deposit of calcium in the marginal brain tissue often in addition to that in the glioma itself the nutritional disturbance extending for a variable distance beyond the actual borders of the tumor.

#### SUMMARY AND CONCLUSIONS

1. A short general review of the occurrence of intracranial calcification is given with the pathologic possibilities. Calcareous deposit may be found in practically every type of primary intracranial new-growth although with the exception of the craniopharyngeal pouch cysts it is probably most common in the gliomas.

2. Hyaline degeneration or other marked regressive changes are not essential to the deposit of calcium in gliomas. It is essentially a chemical rather than a histologic process. The calcareous material is found characteristically in the media and the adventitia of the blood vessels occurring to a much less extent in the cells of the tumor and very rarely in the stroma. The association of calcification in small blood vessels with liquefaction cysts at the margin of the glioma is noted.

<sup>47</sup> Landau, Max. Das diffuse Gliom des Gehirns. Frankfurt Ztschr. f. Path. 5: 469, 1910.



3 The presence of calcification is of value in the diagnosis and localization of gliomas, and further emphasizes the importance of securing satisfactory roentgenograms of the skull in every case in which intracranial tumor is suspected. The distribution of the calcareous material is usually evenly spread throughout the tumor tissue and gives some conception as to its size and relationships. The duration of the symptoms will often suggest the type of glioma that can be suspected; those with a history of from six to twelve months will likely be neuroglaiomas (spongioblastomas), while those of longer duration will more likely be astrocytomas.

4 Because of the small size of the individual masses, calcareous material may be present in a glioma and yet fail to appear in the roentgenogram. Roentgen examination usually reveals an associated thinning of the skull over the tumor, indicating a local rather than a general increase in pressure.

5 As observed either roentgenographically or histologically, the calcareous particles show a variable distribution in the tumor tissue. They may be spread evenly or unevenly throughout the tumor or may be confined to a single dense mass in its more central portions.

6 Calcification in a glioma is an indication of its relative rather than its absolute benignity. A large proportion of our cases showed the variety of glioma considered malignant. The process may apparently occur in any type of the group.

7 Twelve cases are reported. Of the ten growths verified histologically, five proved to be neuroglaiomas (spongioblastomas), three were astrocytomas, one was an ependymal glioma (ependymoblastoma) and one an unclassified glioma, apparently a cerebral medulloblastoma.

8 Actual bone formation was found in one case. In the literature we found the record of but one other case in which bone formation had taken place in a glioma, that of Oppenheim. We report a case of calcification in a cerebellar glioma, the counterpart of which we have not been able to find in literature. This is probably of more relative than actual import, for there is no reason why calcification should not occur in the cerebellar astrocytomas, unless the early production of hydrocephalus brings about the patient's death before the process takes place.

Dr. Rav A. Carter, head of the Department of Roentgenology of the hospital, permitted us to use the roentgenograms shown, as well as his valued report.

# THE CLOSED INTESTINAL LOOP

## I RELATION OF INTRALOOP (JEJUNUM) PRESSURE TO THE CLINICAL CONDITION OF THE ANIMAL \*

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This work was undertaken in an attempt to throw further light on the relation of hydraulic pressure within intected hollow viscera to the clinical course presented. It was pointed out by Van Zwahlenburg<sup>1</sup> that as the distention of hollow viscera takes place by increased pressure from within, the circulation is gradually blocked and effusion into the lumen tends to increase the fluid and pressure there. Necrosis and rupture are the natural sequelae. In most instances the viscus contains many organisms and toxic products which when freed by rupture spread infection and permit of wide surfaces for absorption resulting in death.

It seemed to us that the closed intestinal loop in the dog as introduced by Whipple<sup>2</sup> and his associates, if placed where it was accessible for measuring the intraloop pressure without adding complications to the situation, should lend itself admirably to this investigation. Accordingly the following procedure was used in preparing the animals for this study.

### EXPERIMENTAL PROCEDURE

Entering the peritoneal cavity through a right rectus incision we chose a segment of jejunum with a good mesenteric blood supply which would not be embarrassed when sufficient tension was placed on it to bring the segment to the anterior abdominal wall. The distance of such a segment from the ligament of Treitz varied in different dogs but averaged about 25 cm. In the early experiments we attempted to make the loop approximately 20 cm from the ligament of Treitz.

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\* Submitted for publication March 17, 1930.

\* From the Department of Physiology, University of Oregon Medical School.

\* Aided by Grant 149 (Van Zwahlenburg) of the Committee on Scientific Research of the American Medical Association.

1 Van Zwahlenburg, C. A. Strangulation Resulting from Distention of Hollow Viscera. *Ann. Surg.* **46**: 789, 1907.

2 Stone, H. P., Bernheim, P. M., and Whipple, G. H. Intestinal Obstruction. A Study of the Toxic Factors. *Pull. Johns Hopk'n Hosp.* **23**: 159, 1912.

In some dogs this resulted in a strangulated loop so that such a criterion for its location was abandoned. The length of the segment, too, varied with its mesenteric supply but averaged about 15 cm. After the ends were turned in and the loop had contracted from trauma, it was considerably shorter. A very fine curved intestinal needle and 00 plain catgut were used in closing the ends. Ample inversion (1 cm) was made in order to prevent the end from opening on early postoperative rise of intraloop pressure. The loop was then dropped back into the peritoneal cavity and the continuity of the gastro-intestinal tract reestablished by an aseptic, end-to-end anastomosis. This accomplished, the midline lapp

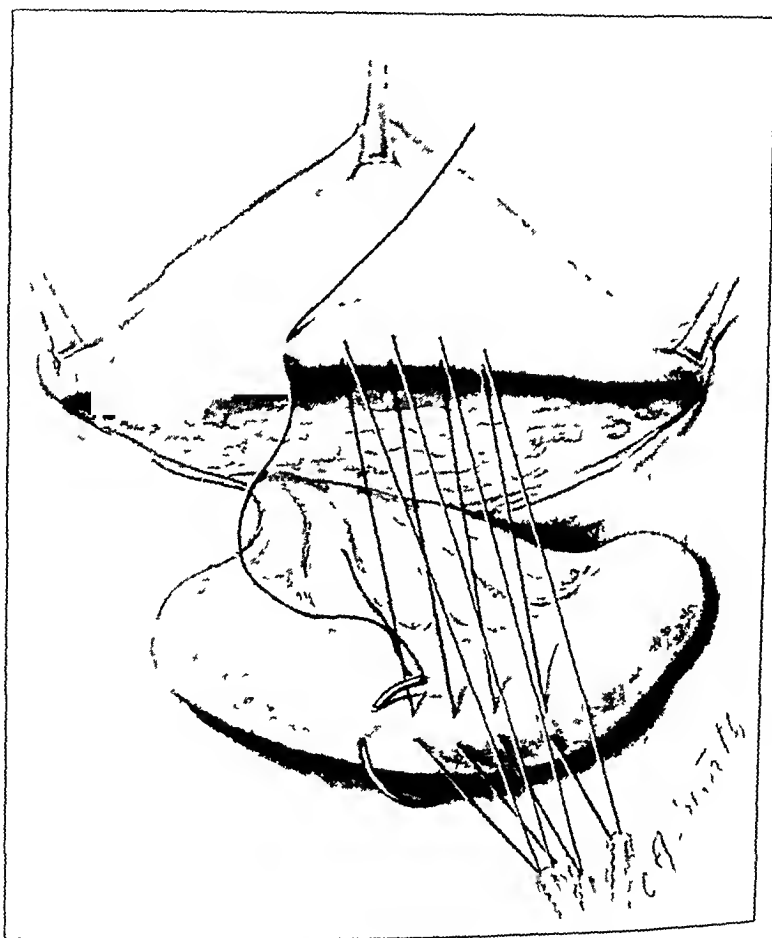


Fig 1—The sutures placed for attaching the loop to the anterior abdominal wall

appendage was dissected back over the midline between the xiphoid process and the umbilicus, giving a traumatized area to which the loop was attached in its midthird portion. Suturing here was done with 0 silk on a very fine curved intestinal needle. Interrupted sutures were used which were passed first through the peritoneum and then through the antimesenteric portion of the intestinal wall. In placing this intestinal stitch, we made no attempt to pick up the submucosa. The submucosa was engaged, it was only in its outermost zone. This is of course contrary to good intestinal surgical technic in that it is the submucosa that can withstand the pressure of suture tension. However, in the dogs used in the early part of the experiment we found that loop perforation from pressure often occurred at the site of one of these sutures. This may well have been due to placement

sutures too deeply, even into the mucosa. Since we have been making a studied attempt to pick up no more than the outermost layer of the submucosa, we have had no perforations at the point of suture. The sutures were all placed before they were tied as shown in figure 1. When the operation was complete, the jejunal loop was held against the anterior abdominal wall as shown in figure 2, and two linen sutures were placed in the skin of the anterior abdominal wall to show the midpoint of the loop attachment. Closure of the right rectus wound was done by the usual three-layer suture method. These loops almost uniformly adhered to the abdominal wall, so that the loop could be punctured at will for the study of loop contents.

After operation, the dogs were kept in separate cages in a warm room. Water was given after forty-eight hours, and milk or hamburger after ninety-six hours. Approximately twenty-four hours following the operation the dog was placed on the operating table and the skin over the area of attachment of the loop cleaned with alcohol. A hypodermic needle (no. 19) was then inserted through this area into the loop. Attaching a sterile syringe, the operator first made sure that

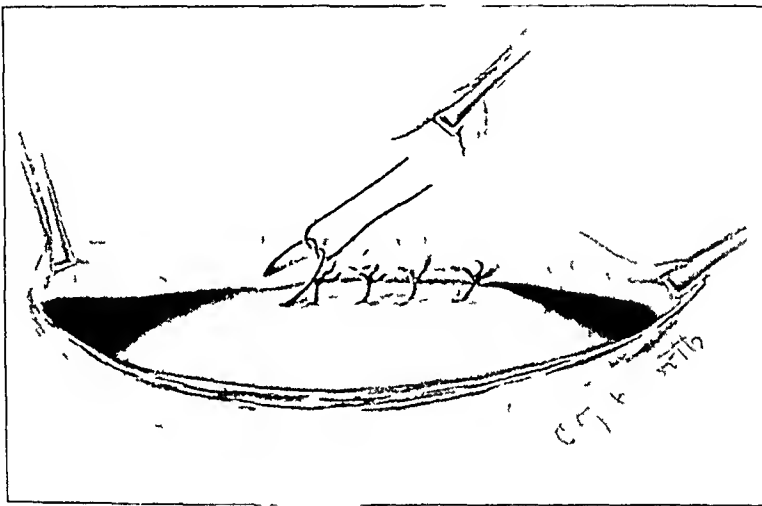


Fig 2—Loop attached to the anterior abdominal wall

the needle was in the loop and the fluid free to flow out. The syringe was then removed and a sterile apparatus attached for measuring the pressure in the loop. This consisted of a straight piece of glass tubing of 3 mm bore and 35 cm long, to which a rubber tube 24 cm long was attached. The quantity of fluid removed from the loop in measuring the pressure was thus at no time sufficient to affect the pressure materially. After the pressure was determined, the fluid was withdrawn with the syringe. This procedure was usually repeated each day for the first three or four days. Evidence thus gained as to the rate at which the fluid formed was used in deciding whether or not "tapping" should be continued at regular intervals.

Fifty-one dogs were used in this study of the jejunal loop. Twenty-three of these died within ninety-six hours. At autopsy, the causes of death were divided as follows. Three had peritonitis from an imperfect end-to-end anastomosis, four had rupture of the loop at one of the stitches used to hold it to the abdominal wall, one died as a result of

anesthesia and three from respiratory infection, three had no fluid removed from the loop, with consequent rupture and peritonitis, nine died in spite of the removal of fluid, owing to the fact that the mesenteric vessels were compressed at the root (strangulation). This, we discovered, after several animals had been lost, could be avoided by choosing a loop lower down in the jejunum. Because of differences in the mesenteric root in different dogs, it became necessary to study the mesentery of a segment to make sure that tension on it (as when brought to the anterior abdominal wall), did not embarrass the circulation at the root.

Sixteen animals were lost in less than thirty days following the operation. Some of these were not tapped for several days before death. The loop had become distended and ruptured before any objective symptoms were noticed. In a few animals gangrenous loops developed in spite of tapping, probably due to embarrassment of the circulation at the root of the mesentery. Three were lost because of infection in the incision, two showed peritonitis due to imperfect end-to-end anastomosis, and one died on the fifth day from ruptured loop, no fluid having been removed at any time.

Of the remaining twelve dogs, three were killed for histologic examination of the loops, three are alive and six died from ruptured loops. The average length of life of this group was more than four months.

#### COMMENT

As is seen from the foregoing description, there are several possibilities for complications. To those enumerated should be added the experimental hazard of tapping the loop. One can miss the loop easily if it is contracted, or the needle, if too long, may go through the loop and carry organisms into the peritoneal cavity. If there has been only a narrow adhesion of the serosa of the loop to the anterior abdominal wall, the needle may miss this area and enter the loop on its free surface. This again furnishes a possible source of contamination of the peritoneal cavity.

We feel, therefore, that, barring the experimental difficulties of the various types mentioned, the simple expedient of keeping down the initial loop pressure is the outstanding factor in the recovery of these animals. At this level in the intestinal tract pressure develops in the closed loop on the first or second day after operation. This may continue for several days even with withdrawal of fluid. It was found necessary in most dogs to withdraw fluid every few days during the life of the animal.

The amount of pressure found in the closed loops varied from 0 to 56 cm. of water. The highest pressures recorded the first few days

following the operation are taken as indicative of the initial loop pressure that might be effective in blocking the circulation. As a result of operative trauma, the tone of the muscularis is greatly decreased and a pressure that would cause little distention normally is now capable of causing marked distention. This combines two factors in producing circulatory stasis, namely, initial loop pressure and stretching of the capillaries. A loop markedly distended by a pressure of 25 or 30 mm of mercury has its circulation partially blocked. This is evidenced by necrosis on the antimesenteric border of the loop. In the accompanying table are recorded the highest pressures found in fifteen dogs the first few days following operation. The average high pressure is 39.5 cm of water or 30.4 mm of mercury. One would expect this to be

*The Highest Initial Loop Pressures\* Recorded Together with the Amount of Fluid Removed from the Loop*

Dog	Pressure, Cm of Water	Quantity of Fluid Withdrawn, Cc	Days Following Operation	Length of Life Following Oper- ation, Days
1	15	50	3	24
6	32	60	2	8
9	30	45	0	96
10	38	51	3	9
11	26	20	2	4
12	30	45	6	171
22	45	55	4	50
31	45	90	2	2
36	12	60	1	4
37	42	75	1	4
38	36	50	2	5
40	46	105	2	4
4	52	75	3	11
44	56	95	3	4
15	28	50	4	4

\* The average loop pressure was 39.5 cm of water.

below the pressure required to block completely the circulation to the loop. In most instances the pressure probably was taken before it had reached a maximum, and in others a small rupture had probably taken place and part of the fluid escaped into the peritoneal cavity, thus lowering the pressure.

In this connection Dragstedt<sup>3</sup> and his co-workers recently studied the amount of pressure necessary to block the circulation in a loop of intestine with the dog under anesthesia. They found this to vary with the level of the loop. In the duodenum from 35 to 40 mm of mercury was sufficient, in the jejunum and ileum from 55 to 65 mm, and in the colon, 95 mm. These were acute experiments, and under such circumstances the actual distention of the loop is not great, owing to the effective resistance of active muscularis. In other words, the

<sup>3</sup> Dragstedt, C. A., Lang, V. G., and Millet, R. F. The Relative Effect of Distention on Different Portions of the Intestine, *Arch. Surg.* **18**: 2257 (June) 1929.

stretching of the capillary hardly enters into the problem. Thus, we feel, is a factor in explaining the wide difference between our observations and those of Dragstedt.

Owings, McIntosh, Stone and Weinberg,<sup>4</sup> by using a tube in one end of an isolated loop and allowing the other end of the tube to protrude through the abdominal wall to which it was clamped, investigated the development of pressure in the loop. They obtained a pressure in duodenojejunal loops of 50 cm of water at the end of twenty-four hours. Only four dogs were used, and these survived from twenty-nine to fifty-four hours.

The clinical symptoms in our dogs in which a closed loop had been made were not marked when the pressure was kept down and the loop did not rupture. Where there were no complications the symptoms were little if any different from those seen in our control animals following intestinal resection and an end-to-end anastomosis of the jejunum. The temperature ranged between 101 and 103 F. There was usually no vomiting and no marked changes in the blood chemistry.

Toxic material from bacterial action is present in the loop in varying amounts at all times. When the loop is not distended and the circulation to it is good there can be very little absorption of this material, or the amount absorbed is detoxified by the liver. Such animals do not differ from normal animals in any demonstrable way, in actions, appetite, temperature or blood chemistry. On the other hand, when the loop becomes distended, objective symptoms are usually present. The dog may have eaten heartily in the evening and twelve hours later may refuse food. The temperature may or may not show a slight rise. The animal is not quite so lively. Of these symptoms the only reliable one is refusal of food. If the animal is tapped, so that pressure is relieved, he may eat at once, if not at once, always within the next hour. A more severe or longer continued distention produces more marked symptoms such as vomiting and depression. On tapping such dogs a large quantity of fluid is found. They are somewhat slower to take food but do so in the course of two or three hours. Even at this time there are usually no significant changes in the blood. If the loop is perforated under this tension, depending on the amount of fluid escaping and its toxicity, the symptoms are slight or the animal shortly becomes moribund. This tendency for a loop to fill with fluid at irregular intervals is seen in most dogs. Tapping may not have been done for several days or weeks, when suddenly the animal refuses food indicating a distended loop. This may occur every day or every other day for a week or ten days, when the fluid gradually ceases to form.

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<sup>4</sup> Owings, J. C., McIntosh, C. A., Stone, H. B., and Weinberg, I. A. Intra-Intestinal Pressure in Obstruction, *Arch Surg* 17: 507 (Sept) 1928.

taster than absorption takes place. The cause of these periodic disturbances in the secretion absorption balance in the loop is not clear. Although it is possible that the disturbance is brought about by irritation from within, it seems more probable that it is due to pressure on the mesenteric vessels by an over distended colon, and that the fluid results from filtration rather than from secretion.

These attacks, even though the animal may have vomited several times, are probably due more to reflex nausea and pain from the distended loop than to absorption of toxic products. This theory is borne out by the facts that (1) at this time the blood chemistry shows little or no change and (2) the animal eats either at once or within two or three hours, all objective symptoms having disappeared.

The flora more or less regularly found in these loops include *Bacillus coli*, *Bacillus welchii* (organisms and spores), enterococci and streptococci. Other organisms have been found but less regularly and in smaller numbers. As the loop becomes older, *B. welchii* disappears and one of the other three types tends to predominate. It seems clear that only a slight inhibitory influence is exerted by the secretion of the loop on its bacterial content. Those organisms that can thrive on the mucus and debris in a slightly alkaline medium battle for predominance. There is some evidence that great numbers of organisms, when present may directly or indirectly cause excess formation of fluid. The rôle of organisms is being carefully studied.

Different investigators have been led to believe that the hydrostatic pressure in closed loops of intestine is an important factor in determining the clinical course of the animals. Sweet, Peet and Hendrix<sup>5</sup> stated the opinion, "that it is only because of such distention and consequent rupture that our animals with closed loops die." Dragstedt<sup>6</sup> and his associates showed that dogs with closed loops washed with astringents would live indefinitely. They made the following statement: "The factor of distention in short closed intestinal loops is of paramount importance in the production of the toxemia, since if the distention is prevented in the majority of cases toxemia does not occur." More recently Dragstedt<sup>7</sup> stated "The toxemia and decrease in blood chlorides is in turn dependent upon distention of the closed intestinal segment. If this distention is relieved by aspiration of the fluid within

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5 Sweet, J. E., Peet, M. M., and Hendrix, B. M. High Intestinal Stasis, *Ann Surg* **63** 720, 1916.

6 Dragstedt, L. R., Dragstedt, C. A., McClintock, J. T., and Chase, C. S. Intestinal Obstruction. II. A Study of the Factors Involved in the Production and Absorption of Toxic Materials from the Intestine, *J Exper Med* **15** 109, 1919.

7 Dragstedt, L. R. Blood Chemistry in Intestinal Obstruction, *Proc Soc Exper Biol & Med* **25** 239, 1928.



the segment, by a needle thrust through the abdominal wall, the toxæmia is relieved and there occurs a proportionate return of blood chloride concentration toward the normal level." Stone and Firor<sup>8</sup> tested the absorption of india ink by the intestine below and above a point of obstruction. In the latter instance only were they able to recover it from the mesenteric glands and lymphatics. They also placed a loop of intestine containing toxic material and distended with air, in Ringer's solution. This solution soon showed toxic properties. Raine and Perry<sup>9</sup> concluded that, "diminishing intra-intestinal pressure in an obstructed bowel prolongs the life of rabbits, because it diminishes secretion and promotes reabsorption." When the closed loop is made available, as described by us, it is possible to get more direct evidence as to this relationship. In our experience, hydrostatic pressure develops in practically all closed jejunal loops. The relief of this pressure permits a normal recovery, provided the circulation is good. There is little or no vomiting unless the loop is distended. Decrease in blood chlorides, typical of clinical obstruction, was not seen in our animals.

Dogs 15, 20 and 31 were killed after 178, 160 and 126 days, respectively, all were in excellent condition at this time. Dogs 15 and 20 had been tapped at irregular intervals since the loop was made, neither had been tapped for two weeks preceding their death. Dog 31 had not shown signs of pressure, and no fluid had been removed from the loop since the fifth day following operation. Grossly, these loops appeared normal. A gray pasty-like material was present in the loops; when this was washed away, the mucosa appeared normal. Except for occasional areas which showed absence of the epithelial covering microscopically, the mucosa appeared essentially normal. Some short and broad villi were present that showed an increased cellular infiltration over that seen in control sections from normal jejunum. The muscularis was uniformly moderately hypertrophied. It is possible that these pathologic changes noted can be accounted for, in part at least, by the accumulated pasty-like material. The needle punctures, also, may have brought about some damage to the mucosa that had not been fully repaired. Histologically the amount of normal mucosa seen so far exceeded the areas of slight pathologic change that one was led to believe that normal functions of secretion and absorption could be carried on. It would seem, therefore, that such loops might lend themselves to various physiologic or pharmacologic investigations.

8 Stone, H. B., and Firor, W. M. Absorption in Intestinal Obstruction. Intra-intestinal Pressure as a Factor, *Tr. South Surg. & Gynec. A.* **37** 173 1924.

9 Raine, F., and Perry, M. C. Intestinal Obstruction. Experimental Studies on Toxicity, Intra-Intestinal Pressure and Chloride Therapy, *Arch. Surg.* **19** 478 (Sept.) 1929.

The specimens obtained from the loops were tested regularly for sucrase and erepsin. These observations will be reported later with results in loops at different levels of the small intestine. It should be stated here that the concentrations of these enzymes vary only slightly in a given animal while in good condition. However, if the loop becomes distended with a large amount of fluid, the concentration of enzymes is usually low. This would seem to indicate that in such instances the accumulated fluid may be the result of filtration rather than of secretion.

#### SUMMARY AND CONCLUSIONS

- 1 A method of attaching a closed intestinal loop to the anterior body wall where it can be readily reached with a hypodermic needle is described.

- 2 Dogs with closed jejunal loops, with the continuity of the intestinal tract reestablished, can be kept alive indefinitely, provided the pressure in the loop is kept down by aspiration of the fluid.

- 3 Such animals with closed jejunal loops, barring complication, do not show the clinical symptoms of obstruction. Vomiting is seldom seen, and the blood chlorides do not undergo significant change.

- 4 By permitting distention and pressure to take place in the closed loop, vomiting is precipitated, refusal of food is an invariable symptom. The animal is immediately relieved and will eat almost at once following aspiration of the fluid. This would seem to prove that the symptoms are due to reflex nausea and pain from distention of the loop. Although there is probably some absorption of toxins at this time, it is not the important factor in producing the symptoms observed.

- 5 The flora found in the jejunal loops consists predominately of *B. coli*, *B. welchii*, enterococci and streptococci.

- 6 The loops in fully recovered animals appear to be essentially normal and should in some ways be superior to the Thiry fistula for the investigation of problems of secretion and absorption.

# SYMPATHECTOMY BY ARTERIAL EXCISION\*

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Until the surgeon began to think of bone as a living fabric with qualities other than its hardness and potentialities beyond its mechanics, progress in the rational treatment for diseases and injuries of the skeleton could not proceed. A corresponding total physiologic conception of the peripheral vascular tree has been slow in developing. The peripheral vessels have too long been thought of as more or less elastic tubes of differing calibers, responding only to the mechanical forces developed from the pulse wave and the succeeding elastic recoil. They are not thought of under all circumstances as living structures responding in their own right to nerve impulse as well.

In the light of the rapidly increasing knowledge of the vegetative nervous system, certain aspects of vascular disease are now looked at with a more seeing eye. In Raynaud's disease, the vasospastic elements of thrombo-angitis obliterans, the vasoconstrictor and vasodilator effects of various physical agents, such as cold and heat, etc., the sympathetic impulse is recognized and made use of in everyday thought and action. The purpose of this paper is to call attention to a factor in vascular disease in which the sympathetic impulse may well play an important part, but in which nerve influence has been somewhat ignored, namely, in the development of a collateral circulation following the obstruction of major vessels.

It is interesting that slight attention has been paid in this country to the possibility of increasing by means of an attack on the sympathetic nervous system the amount of blood passing through collateral channels after arterial ligations. Discussions in the literature of problems of collateral circulation contain no reference to the sympathetic innervation. The Hodgen Lecture<sup>1</sup> of 1929 is an example. In this scholarly and closely reasoned discussion of the effect of ligation of the veins on the collateral circulation following arterial occlusion, Brooks nowhere

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\* Submitted for publication, March 17, 1930.

Read before the Richmond (Va.) Academy of Medicine, Feb. 11, 1930.

<sup>1</sup> From the Department of Surgery and Gynecology, The University of Virginia School of Medicine, from St. Louis City Hospital No. 1, and from Barnes Hospital, St. Louis.

1 Brooks, Barney. Surgical Application of Therapeutic Venous Obstruction. Arch. Surg. 19 1 (July) 1929 (The Hodgen Lecture of the St. Louis Surgical Society, Jan. 15, 1929).

makes mention of possible sympathetic influence Halsted, in 1920<sup>2</sup> three years after Leriche's first publications<sup>3</sup> on the perivascular sympathectomy of Jaboulay, was the first observer in this country to note possible effects on the collateral circulation of a procedure involving ablation of the perivascular sympathetic He observed a marked hyperemia of the arm following excision of a large subclavian aneurysm and definitely ascribed this result to the removal of sympathetic fibers with the sac

Before discussing clinical phases of this problem, it would be well to review briefly present knowledge on the motor innervation of the arteries Details of sensory innervation of central connections and of the question of antidromic conduction need not be allowed to cause con-

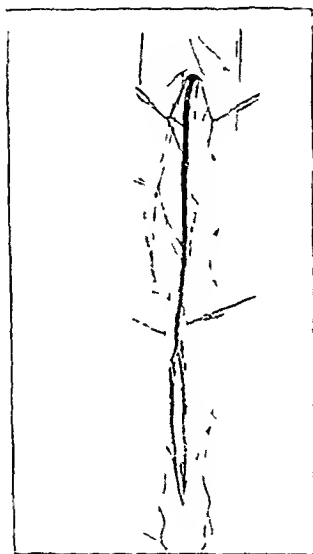


Fig 1—Dissection of the lower extremity, showing distribution of nerves to the large arteries Note that sympathetic branches to the vessel pass from the peripheral nerve to the artery wall at intervals (Reproduced from Kuntz *The Autonomic Nervous System*, p 138)

fusion in the present discussion All blood vessels, including arteries, veins and capillaries, receive sympathetic nerve fibers These fibers are carried to the vessels in the peripheral nerves and distributed to their walls at intervals along their courses It has been fairly well shown that few, if any, fibers pass distally from the trunk in the coats of the vessels (fig 1) The nerves reaching an artery are distributed

<sup>2</sup> Halsted Elevation of Temperature of Hand Following Excision of Subclavian Aneurysm, *Bull Johns Hopkins Hosp* **31** 219, 1920

<sup>3</sup> Leriche, R De la sympathectomie periarterielle, *Presse med* **25** 513 1917 Leriche, R and Heitz, J Des effets physiologiques de la sympathectomie peripherique *Compt rend Soc de biol* **80** 66 1917 *ibid* p 160

to all coats, the greatest number lie in the adventitia. These, facts in outline, make up the anatomic background for this discussion. Kuntz in his recent book on the autonomic system,<sup>4</sup> summarizes present knowledge in greater detail.

Over these nerves come impulses from the central nervous system representing the penultimate stage of reflexes and resulting in vasoconstriction or vasodilation. The constrictor influences predominate so that division of the sympathetic nerve to a part results in vasodilation. Curiously enough, the removal of the adventitial fibers from an artery also results in vasodilation of the entire extremity below the point of attack. This result contradicts the ordinary conception of nerve influence. As I have already remarked, no through fibers are destroyed by this procedure. There is no anatomic basis for predicting any effect whatever, except on the segment of artery from which the plexus is removed. This clearcut paradox, taken with the further fact that experimental reproduction of the phenomenon in laboratory animals has not been accomplished, has done much to retard the general acceptance of Leriche's procedure. The bizarre quality of the reaction is further emphasized by the fact that in isolated instances Leriche has reported vasodilation in the opposite extremity alone in both the operated extremity and its mate, and indeed, in all four extremities following periarterial sympathectomy of a single vessel. Again, at times no reaction may occur.

Much theorizing has been done on this subject but no satisfactory explanation has been proposed. The clinical fact exists, nevertheless that the stripping of the adventitia from a major artery results in most instances in a striking physiologic sequence: first, the primary effect of a few hours' duration, consisting in intense vasoconstriction to the degree of obliteration of the peripheral pulse, and second the secondary phase, immediately succeeding, of vasodilation, increased surface temperature and increased volume flow of blood lasting over a period of weeks. This phenomenon has been evoked in a sufficient number of clinical cases to make its recognition sound. No anatomic contradiction can invalidate it. It does not need the support of comparative physiology. The therapeutic effects of the procedure are familiar in certain selected groups of cases, but these are not germane to the present discussion.

Much time has been spent in the laboratory in unsuccessful attempts to reproduce the phenomenon. Leriche<sup>5</sup> proposed a possible

4 Kuntz, A. *The Autonomic Nervous System*, Philadelphia, Lea & Febiger 1929.

5 Lehman, Edwin P. *Periarterial Sympathectomy. An Experimental Study*. *Ann Surg* **77** 30 (Jan) 1923.

6 Leriche, R. *Sur l'étude expérimentelle, etc. de la sympathectomie artérielle*. *Presse med* **30** 1105 (Dec 23) 1923.

explanation Man, in the course of his development, has needed to compensate for his hairlessness by an increased sensitiveness of his vasomotor mechanism External changes in temperature do not strike the sensory endings in the skin beneath the thick growth of hair of animals as they do those in the nude skin of man Man, therefore, has developed a control of his blood vessels more highly specialized and consequently with somewhat different reactions The discrepancy is explained on phylogenetic grounds It is an ingenious idea on which it is not necessary, perhaps, to pass critical judgment

The usual method of removal of the perivascular sympathetics is, of course, the stripping operation on the otherwise intact artery In selected cases there is an alternative method, namely, the excision of a segment of the whole vessel, the operation of arteriectomy It is my purpose to present clinical evidence suggesting that arteriectomy in the presence of arterial occlusion has a favorable influence on the distal circulation If such favorable influence can be shown, the cause of it need not be sought further than in the fact just mentioned Arteriectomy includes, of necessity, sympathectomy The reactions shown by the two operations are comparable, differing only in that in the former less blood is available for the dilated vascular tree than in the latter I propose, more or less tentatively, the excision of a segment of artery in any case of complete arterial occlusion of a major vessel with a view to obtaining a vasodilator effect on the collateral channels This proposition has been made by Leriche on the basis of early experience in cases of causalgia, trophic change and edema, associated with an obliterated artery In his later publications,<sup>7</sup> Leriche has carried the proposition still further, including types of disease that I shall subsequently discuss However, his approach to the problem is somewhat different from that in the present paper He does not propose to influence the collateral circulation by arterial excision, but rather to excise irritated sympathetic fibers which he believes are creating vasospastic conditions He therefore takes the position that he is attacking sympathetic disease directly A sentence from one of his recent discussions of the problem is illuminating "An occluded artery is no more an artery, but a plexus of sympathetic nerves in an abnormal condition"<sup>7</sup> Although this point of view bears an intimate relationship to the point of view now being considered, it cannot well be included in this thesis without undue confusion

The question arises as to the difference between excision and ligation with division of the artery as ordinarily practiced It might be thought that ligation with division would satisfactorily block vasomotor

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<sup>7</sup> Leriche, R, and Stricker, P Observations on Juvenile Obliterating Arteritis, *Brit J Surg* 16 496 (Jan) 1929

impulses in the adventitia. However, as has already been noted, the effect of perivascular sympathectomy cannot be explained on the basis of nerve block. Apparently, whatever the explanation may be, there must be removal of a considerable number of fibers, some break, perhaps in a complicated series of reflex arcs. Furthermore, the effects I am about to illustrate, so far as I am aware, have not been observed without excision as well as division.

The operation of arteriectomy should be considered on the aforementioned grounds in any case of complete arterial occlusion in an extremity, whether from disease, from trauma or from surgical ligation in the treatment for disease or trauma. One must except those cases of embolism in which embolectomy can be practiced within twenty-four hours. In my own experience, it has been employed associated with ligation for accidental trauma, in the treatment for arterial thrombosis, thrombo-angitis obliterans and for false aneurysm. It has not been completely successful in averting gangrene, nor has the physiologic reaction of distal hyperemia been uniformly observed. In enough instances, however, definite hyperemia has resulted, even though there has been a previous ischemia, to suggest a sound theoretical basis for the operation. It is to be remembered, as will be emphasized later, that in most instances it is harmless.

#### REPORT OF CASES

In considering my cases, I shall group them into the four divisions already named, with discussion of each group as a separate problem.

*Group I—Ligation for Trauma*—CASE 1—The record of this case, unfortunately, is not available. In 1923, Bardon and Mathey-Cornat<sup>8</sup> reported striking results in the rapid healing of chronic ulcers of the leg following periarterial sympathectomy. I had at that time an aged patient in the ward of the St. Louis City Hospital suffering from enormous dirty sluggish ulcers on the lower part of both legs, for which double amputation had been suggested. I attempted a periarterial sympathectomy on the femoral artery of the side presenting the large ulcer. The artery was almost completely calcified, and during the manipulation it ruptured. Ligation was necessitated. In the course of this procedure the ligature cut through several times, so that finally a considerable segment of the artery was destroyed and excised. This was, of course, a proceeding forced by accident without purpose at the time. Striking improvement in the ulcer on the side of the operation with the establishment of active granulation tissue and the beginning advance of epithelium was observed before the patient left the hospital about ten days later, against advice. There was never any disturbing coolness of the foot. That this result should have occurred in any patient with advanced arteriosclerosis after destruction of the main blood supply to the leg, was interesting. The most probable explanation is the performance of sympathectomy in the process of excision of the damaged arterial segment.

<sup>8</sup> Bardon and Mathey-Cornat. Periarterial Sympathectomy in Chronic Ulcers of the Leg, Lyons chir. 20 694, 1923.

This case is not presented as suggesting arterial excision for chronic ulcer or for arteriosclerotic ischemia. It is presented as an example of a traumatic division of a major vessel in which arterial excision was performed, albeit without purpose, and in which there was clinical evidence of improved circulation below the level of occlusion.

CASE 2—A white man, aged 26, was shot through the upper part of the left thigh. The bullet injured the femoral artery and the vein just below Scarpa's triangle. There was coolness of the left foot and absence of palpable pulsations in the vessels. At a first operation by another surgeon shortly after the shooting, the exposure of the actual injury was frustrated by extremely active bleeding and a marked state of shock. The patient had lost considerable blood before admission. It was necessary to control the bleeding by packing the wound tightly.

During the course of the next twenty-four hours, his thigh became enormously swollen, and marked cyanosis developed in the lower part of the leg, which remained warm. The foot was pale and cool. The cyanosis was of an intense purple tinge, resembling that seen in traumatic cyanosis of the head and neck following crushing of the chest. The superficial veins were filled with blood. It was felt that perhaps the tight packing by pressure on the veins might account for a part of these phenomena. Apparently, at least, some blood was reaching the lower third of the lower part of the leg.

Following transfusion, twenty hours after injury, I reopened the wound and found the femoral artery and vein torn. Thrombosis had occurred, and the artery was not pulsating below the point of injury. Over an inch of the femoral artery and a corresponding amount of the damaged vein were excised. Large incisions in the fascia lata were made to relieve tension.

Following the operation there was no improvement in the patient's general condition, and he died five days later in uremic coma. There was no infection of the wound. Postmortem examination was not permitted.

There were changes in the local condition that may or may not have had significance. The day after the excision of the artery, there was a definite improvement in the area and degree of cyanosis of the lower part of the leg. The area was decreased in size by at least one-third, but the decrease was at the lower margin. The cyanosis was somewhat lighter in color. Warmth continued. The foot remained ischemic and before death early gangrene was established there.

It is impossible to ascribe these results to the arterial excision. Indeed, it is impossible to interpret the appearances with any clarity. The effect of the tremendous tension in the thigh from hemorrhage and packing cannot be overlooked. The case is presented as an example of a type of injury in which ligation is obligatory, in which excision is harmless, and in which this procedure may be done only with the hope that favorable results may be obtained.

*Group II—Arterial Thrombosis*—CASE 3—A white, married woman, aged 38, with rheumatic heart disease accompanied by mitral stenosis and auricular fibrillation, had had an embolism of the right popliteal artery about five days before entrance. The embolus had supposedly originated in an auricular thrombus. The history suggested a rider embolus at the aortic bifurcation slipping later into the right vessel. She had had a possible cerebral embolism five months previously.



On admission, there was found coolness of the right leg from the knee down without palpable pulsation in dorsalis pedis or posterior tibial arteries. There was a bluish, mottled discoloration of the right heel and of the plantar surface of the right metatarsal region.

For two days there was little change in the local condition. During the third day there was rapid advance in the signs of ischemia. Change of color was evident over the lower part of the leg, and the calf was indurated and swollen. Pain was excessive. The common femoral artery, previously palpable in the groin, could not be felt. The external iliac was palpable.

It was felt that thrombosis was extending rapidly up the vessel. With the patient under scopolamine-morphine supplemented by infiltration anesthesia, the common femoral was exposed at Poupart's ligament. The pulsation of the external iliac was traced down to this point. Here the vessel was ligated, and the entire common femoral artery, which was completely thrombosed, was excised (figs 2 and 3). The excision included the first 5 mm of both the femoral artery and the deep femoral artery. The latter bled, demonstrating some collateral circulation. This excision was done as a deliberate attempt to influence the collateral flow by sympathectomy.

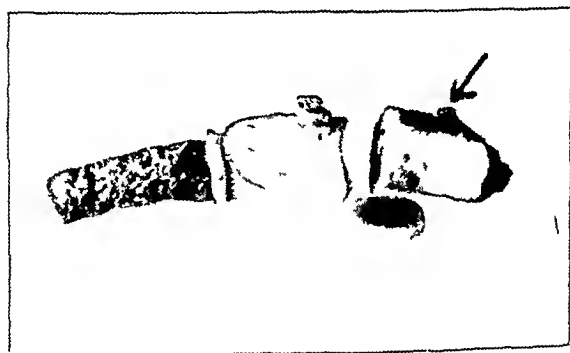


Fig 2—Gross specimen of common femoral artery removed in case 3. An oblique view of the cross-section is shown in figure 3. The arterial wall has contracted to little more than one-half its original length, barring a large part of the thrombus. The arrow points to the stump of the deep femoral artery. The obliteration of the vessel by thrombus is complete.

There was undoubted improvement of the circulation of the lower part of the leg following this operation. The discoloration in the upper portion of the leg disappeared and was replaced by a normal color. This area also showed recovery of warmth for the first time since admission to the hospital five days before.

The distal half of the lower part of the leg did not show improvement. A line of demarcation developed at about the middle of the lower part of the leg, well below the upper limit of the area where gangrene had earlier impended. Although it would have been interesting to have observed further changes, pain and toxemia became so extreme that supracondylar amputation was obligatory on the succeeding day. This was accomplished without incident under spinal anesthesia.

Convalescence proceeded uneventfully for a week, except for slight necrosis of the stump. On the seventh day the patient suffered from embolism of a cerebral vessel and of the left popliteal artery and promptly succumbed. Autopsy was not obtained.

Although gangrene was not averted and the outcome was amputation, the immediate improvement following arteriectomy was striking. The operation made no change in the mechanical conditions of the circulation, the artery was completely blocked before operation, and the vein was not disturbed. The probable explanation for the definite increase in warmth and improvement in color of a part of the extremity must be sought in the effect on the circulation of the incidental sympathectomy.

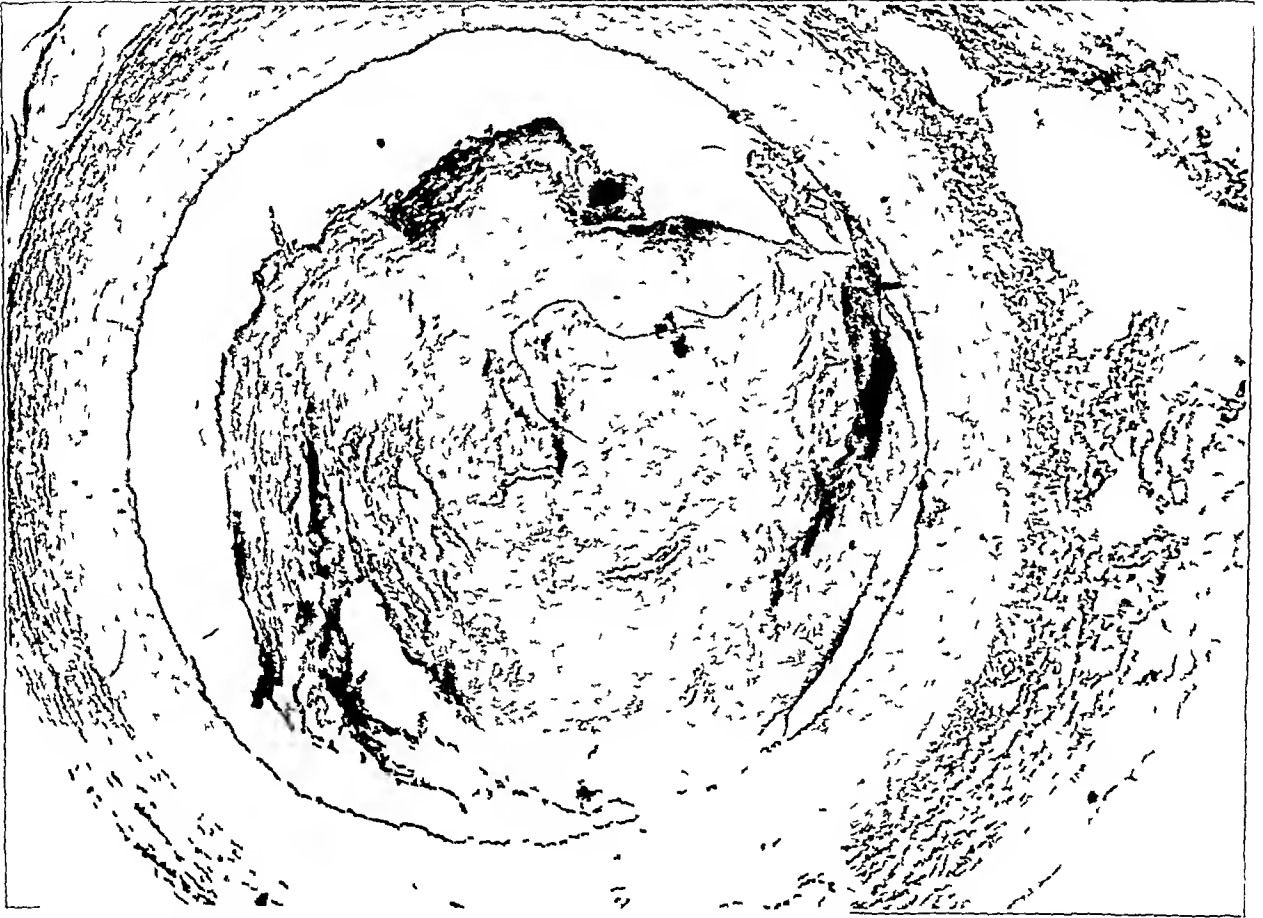


Fig 3—Cross-section of vessel shown in figure 2. Differential shrinkage has occurred so that the thrombus does not appear to block the lumen completely. Examination of the gross specimen reveals this as an artefact.

*Group III—Thrombo-Angitis Obliterans*—CASE 4—A white man, aged 54, came to the hospital in October, 1927, suffering from typical thrombo-angitis obliterans of four years' duration, worse in the right leg. Although claudication had been present, rest pain of an excruciating degree was the predominant symptom. During the first days of observation, a migratory phlebitis was present. No vessels were felt in either foot. The patient was treated by the internists with irradiation of the lumbosacral area. Two months later he returned with practically no change in symptoms but presenting a superficial ulcer of the right heel. In

addition, he suffered from chronic myocarditis with auricular fibrillation and impending decompensation

It was decided to try the procedure described by Lewis and Reichert,<sup>9</sup> namely, the ligation of the femoral artery in Hunter's canal for the purpose of encouraging collateral circulation through the deep femoral. The improvement which Lewis has described in several cases he attributes to the mechanical effect of shunting the force of each pulse wave into the alternative channel. In his descriptions of the operation Lewis mentioned excision of a portion of the vessel as a part of the procedure, but did not emphasize this element. It is done to obtain material for microscopic study.

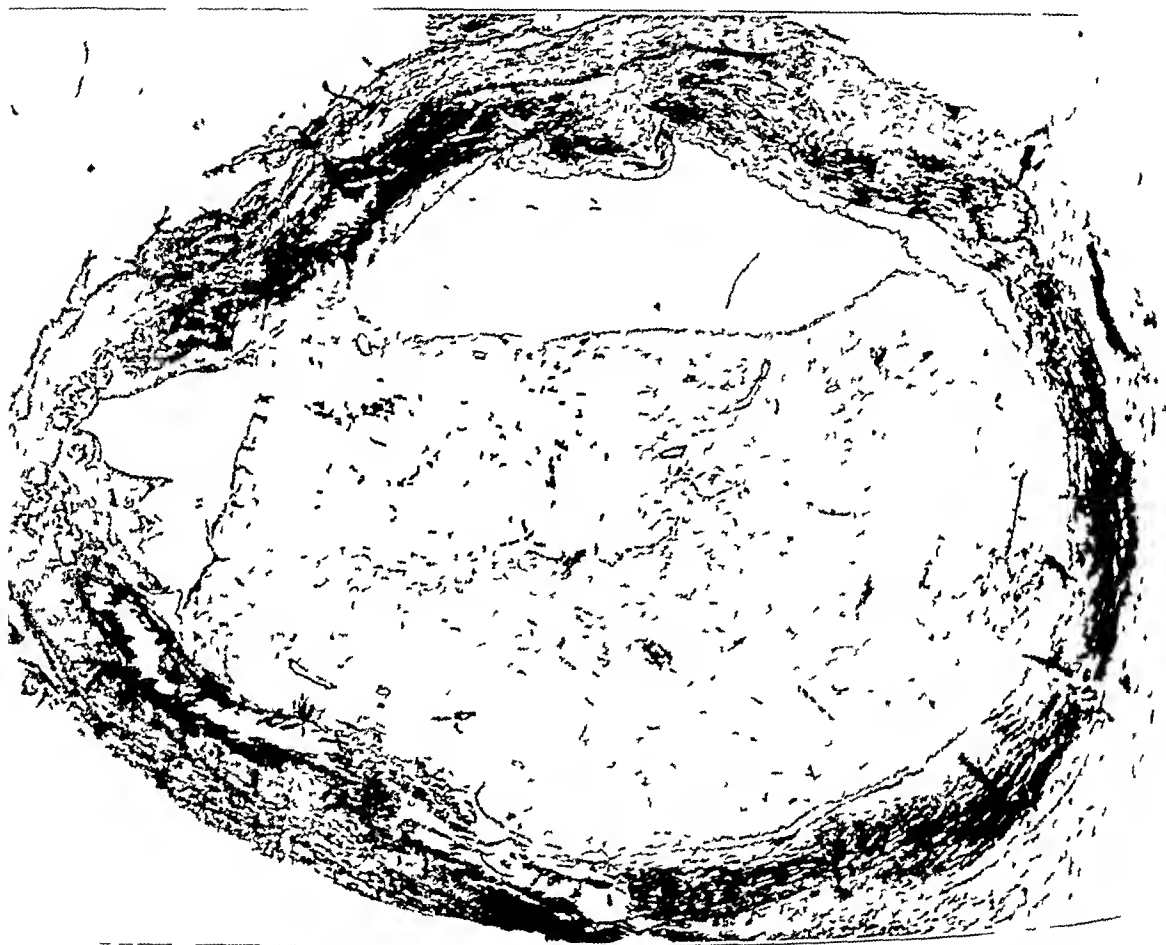


Fig 4—Cross-section of femoral artery removed in case 4. The characteristic changes of thrombo-angitis obliterans are seen. In the gross, before fixation, the open channel shown was considerably smaller, being observed only as a thin slit between thrombus and vessel wall, which were actually in contact.

About 1½ inches (37 cc) of both femoral artery and vein were therefore excised under local anesthesia. Both vessels were resected, because the tremendous perivascular inflammatory process prevented separation and identification of artery and vein. Microscopic study of the excised segments showed almost complete obliteration of the artery by an organized thrombus (fig 4). The tissue changes were typical of thrombo-angitis obliterans.

<sup>9</sup> Lewis and Reichert. The Collateral Circulation in Thrombo Angitis Obliterans, *J A M A* 87 302 (July 31) 1926.

The day following this operation, the patient reported a subjective feeling of warmth in the foot and leg. In his own words, it felt as if "the blood were trying to force through." The continuous pain was relieved and was replaced by a stabbing pain. There was a marked increase in the surface temperature of the foot. The return of color following obliteration of the capillaries by pressure was more rapid in this foot than in its mate. These changes were definite and lasted about four weeks. The ulcer bled freely during this time and diminished somewhat in size. Pain returned early and became a major factor in the care of the patient. The dorsalis pedis pulse was felt on one occasion.

After four weeks pain continued to increase, and the ulcer began to spread. Amputation above the knee became necessary, and an uneventful convalescence followed.

The obliteration of the lumen of the artery was so nearly complete that the mechanical effect of blocking the small amount of blood that could find its way through the remaining channel of the femoral artery must have been inappreciable. The pressure in the deep femoral artery probably was not elevated to a significant degree. Furthermore, the hyperemic reaction was too prompt to postulate mechanical dilation of the collaterals as a cause. The conclusion is forced that the effect followed the incidental removal of sympathetic fibers in the coat of the artery.

CASE 5—A Greek, aged 39, entered the hospital in June, 1929, with dry gangrene of the right foot. Beginning two years previously, he had had three amputations of the left foot and leg. The first was an excision of the fifth metatarsal and little toe for bone necrosis, the second was an amputation at the junction of the middle and upper thirds of the tibia for spreading gangrene, the third was a supracondylar amputation for unhealed stump. At this time a clinical and pathologic diagnosis was made of thrombo-angitis obliterans. Nearly a year before the last admission, gangrene began in the remaining right foot and slowly spread until on entrance it involved practically the entire foot distal to the astragalus. Pain was not marked until shortly before entrance. The lower part of the leg was cool, cyanotic and edematous. The popliteal and distal pulses could not be felt. The common femoral was easily felt. The femoral pulse could be traced part way down the thigh with great difficulty, in spite of extreme atrophy of the musculature.

In this case amputation of the foot was obligatory, but it was exceedingly desirable to save the one remaining knee joint. It was certain that amputation could not be successfully performed below the knee in the existing state of circulation of the lower part of the leg. With the experience of the last case in mind, the Lewis procedure was performed in the hope that the circulation would improve sufficiently to permit the conservative amputation. On this occasion arteriectomy was done, not based on the mechanical conception, but with the express purpose of accomplishing sympathectomy. A portion of the fused artery and vein, about 2 inches (5 cm.) long, was excised. Shortly after operation, the patient noted a sensation of increased warmth in the leg. This was readily confirmed by palpation. The cyanosis disappeared, and the elevated surface temperature remained. There was no improvement in pain. The gangrenous area became moist on the day following arteriectomy.

The evidence of improved circulation seemed to justify an upper tibial amputation, although ultimate healing of the stump could not be predicted with any con-

fidence An amputation at the lower border of the upper third of the tibia was performed six days after the arteriectomy The wound showed moderate necrosis About two weeks later it was necessary to perform supracondylar amputation for persistence of unbearable pain and failure of the wound to heal The final amputation stump of the thigh healed without incident

In this case also, examination of the excised artery showed the possibility of practically no mechanical effect The lumen was completely filled with thrombus which under the microscope showed a few

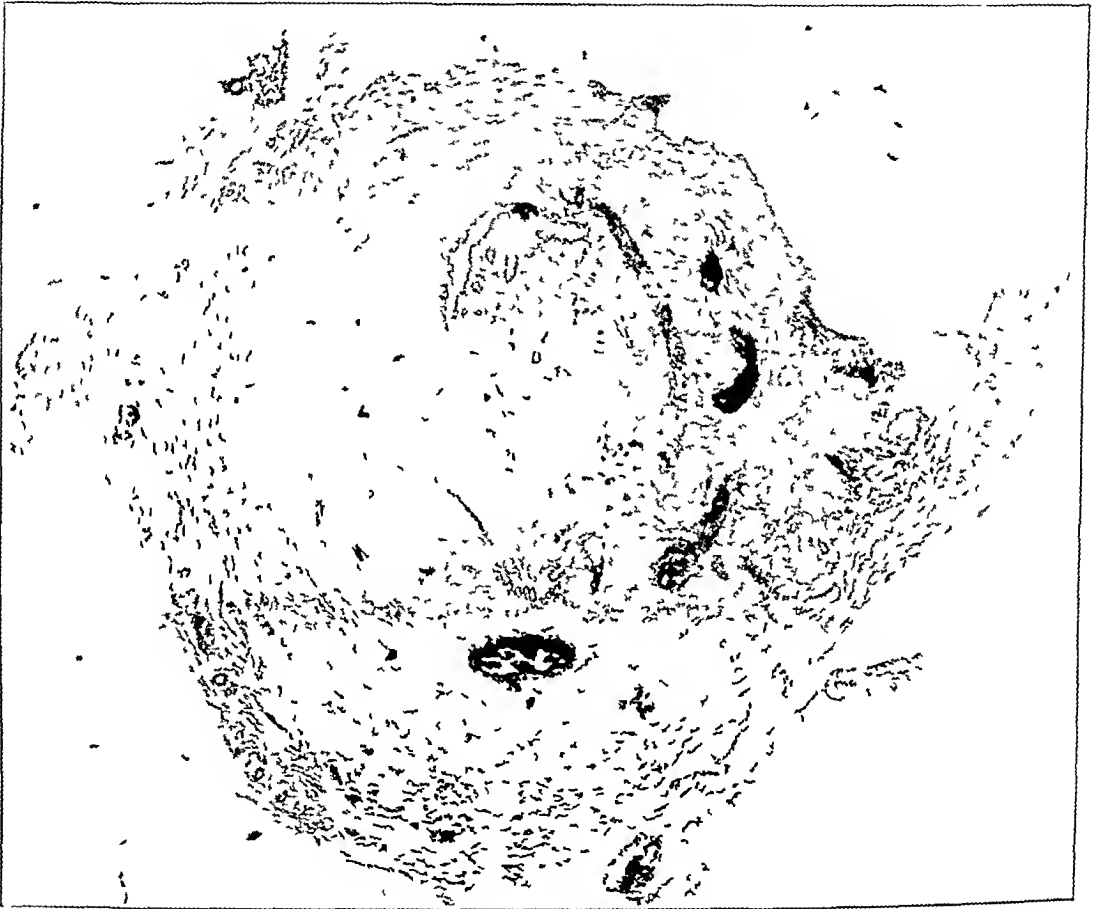


Fig 5—Cross-section of femoral artery removed in case 5 The characteristic changes of thrombo-angitis obliterans are recognized The complete blocking of the lumen by organized and slightly canalized thrombus is obvious

minute channels (fig 5) In this case also, the hyperemia was too prompt to permit a mechanical explanation of the improved distal circulation

The unmistakable clinical evidence of improved circulation in these two cases following arteriectomy, even though amputation was avoided in neither bears out Lewis' experience I offer, however, a different interpretation of the results It seems more probable that an incidental sympathectomy explains the phenomena Both cases had practically

completely obliterated arteries, both cases showed immediate improvement in circulation following the excision of the vessels. In neither case could any significant alteration in proximal pressure have been accomplished by the blocking of the blood current.

*Group IV—Traumatic Aneurysm*—CASES 6, 7 and 8—These three cases need not be described in detail, because in none of them is there any ground to affirm a favorable influence by arteriectomy. In each of them ligation above and below the sac of a false aneurysm was necessary on account of either extensive injury to the vessel or the density of scar tissue about the vessel. One was an acute traumatic aneurysm of the ulnar artery, one a traumatic aneurysm of the popliteal artery of long standing and one a similar aneurysm, even more chronic of the femoral artery. In each case the segment of artery between the ligations was excised. In all three cases distal circulation was unimpaired after operation.

The point in mentioning these cases is to put on record another variety of vascular disease in which the proposed principle can be safely applied.

#### COMMENT

The cases in these four groups have in common the element of ligation of a major artery. In none of them could the ultimate usefulness of the vessel as a blood channel be hoped for. In none of them could the excision be harmful. In at least four, there appeared evidence of improvement in the distal circulation following the excision of a segment of the occluded artery.

The mechanical factors in the development of collateral circulation cannot be dismissed without recognition. The ligation of an accompanying vein as advocated on clinical grounds by Makins<sup>10</sup> and on experimental grounds by Brooks and Martin<sup>11</sup> must not be neglected. Furthermore, postural treatment, protection and heat must continue to be employed as useful agencies in ischemia. I do not propose that this operation replace tried measures.

The excision of an artery is not proposed when there is the possibility of danger. Danger of destroying collateral channels may exist in the excision of the walls of a true aneurysm and possibly of a false aneurysm as taught by Matas<sup>12</sup>. It is improbable that collateral channels existed in the badly scarred arterial walls of the two cases of chronic false aneurysm previously cited. In neither case was the sac

10 Makins, G. Influence Exerted by the Military Experience of John Hunter. *Lancet* 1: 249, 1917 (The Hunterian Oration).

11 Brooks, B., and Martin, K. A. Simultaneous Ligation of Vein and Artery. *J. A. M. A.* 80: 1678 (June 9) 1923.

12 Matas, R. in Keen. *Surgery*. Philadelphia: W. B. Saunders Company, 1909, vol. 5, p. 269.